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File No.: T 0594/92 - 3.4.2

Application No.: 84 307 264.6

Publication No.: 0 141 607

Classification: G02C 13/00, C11D 7/42, A61L 2/18

Title of invention: Improved method for enzymatic cleaning and disinfecting contact lenses.

D E C I S I O N
of 1 October 1993

Applicant: -

Proprietor of the patent: Bausch & Lomb Incorporated

Opponent: Allergan, Inc.

Headword:

EPC: Art. 56

Keyword: "inventive step - yes".

Headnote
Catchwords

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0594/92 - 3.4.2

D E C I S I O N
of the Technical Board of Appeal 3.4.2
of 1 October 1993

Appellant: (Opponent)
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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office dated 29 April 1992 concerning maintenance of European patent No. 0 141 607 in amended form.**

Composition of the Board:

Chairman: E. Turrini
Members: C. Black
L.C. Mancini

Summary of Facts and Submissions

I. European patent No. 0 141 607 (application No. 84 307 264.6) was maintained in amended form by the Opposition Division on the basis of a set of claims of which Claim 1 reads as follows:

"A method of (1) cleaning contact lenses of proteinaceous and other deposits using a proteolytic enzyme in aqueous solution, and (2) disinfecting the contact lenses, characterized in that it is a single step method providing simultaneous cleaning and disinfection which comprises placing the lenses in a solution comprising the proteolytic enzyme dissolved in water and then **subjecting the solution and lenses to a heating cycle consisting of a heating phase followed by a cooling phase, said heating phase consisting of gradually elevating the temperature of the solution from ambient temperature to a maximum temperature between 60° and 100°C and then maintaining said maximum temperature for not more than 20 minutes, the total time for which the lenses are heated at** between 60° and 100°C **being** 60 minutes or less, sufficient to clean and disinfect the lenses"

II. In the course of the opposition the following documents were cited, series A by the Opponent (Appellant) and series B by the Patentee (Respondent):

A1: Hisao Magatani:, Acta: XXIV International Congress of Ophthalmology - San Francisco, October 31 - November 5, 1982, Vol. 2, page 1132 to 1135, published by J.B. Lippincott Co.

A2: DE-A-2 854 278

A3: R.M. Hill & J. Goings: **Contact Lens Forum**, September 1980, page 54,55

A4: Japanese patent application No. 73/113 233 published as No. JP-A-50 064 303,, with English translation received 7 October, 1989

A5: US-A-3 910 296

A6: K. Bhadur and R. Chandra Sinha: Enzymologia, XX, No. 1, 2 to 20 (1957)

A7: M. Bares et al. Scientific Papers of the Prague Institute of Chemical Technology, E45, 97-110 (1976)

A8: US-A-4 285 738

A9: K. Aunstrup: "Economic Microbiology" Vol. 5, "Microbial Enzymes and Bioconversions", page 49 to 69, Academic Press, 1980.

B1: A.J. Philips, The ophthalmic optician (The Contact Lens Review), 20, No. 11, 375 to 388 (May 24, 1980)

B2: Bausch & Lomb: Patient Instructions for wearers of Soft Contact Lenses, revised 1/81

B3: Microbiological Guidelines of FDA, May, 1980 concerning sterilization of contact lenses

B4: US-A-3 623 956

B5: US-A-3 632 957

B6: R.A. Moore *et al.*, Contacto, March 1980, 23 to 30

B7: T. Bailbaut *et al.*, Exp. Eye Res., 53, 153 to 165 (1986)

B8: extracts from transcript of trial Allergan/Alcon & Observations filed by Allergan on 21 November 1991 in the opposition proceedings relating to European Patent number 0 219 220.

B9: H.W. Hind, Contact Lens Forum, November 1979, 17-27

B10: Observations filed by Allergan on 14 September 1990 in the opposition proceedings relating to the above mentioned opposition case EP-B-0 219 220

III. Briefly, the Opposition Division held that A1, the document on which the Opponent most relied, could not be interpreted as suggesting a one-step process for enzyme treatment and heat-disinfection of contact lenses, even when general knowledge at the priority date of the patent in suit, as evidenced by other documents cited during the proceedings, was taken into consideration. The Division accepted that the average skilled person would have been deterred from combining enzyme treatment and heat-disinfection, *inter alia* because of the risk that heat-denatured protein would remain adhered to the lens and that residual enzyme might have a harmful effect on the user's eyes. The Division also observed that none of the cited documents relating to enzyme treatment at above ambient temperature disclosed the gradual increase in temperature to the treatment temperature required by Claim 1, but rather that the enzyme solution was heated to the required temperature before the lenses were brought into contact therewith.

IV. The present appeal lies against this decision. With the grounds for the appeal the Appellant submitted two further documents:

A10: Busschaert *et al*: Applied and Environmental Microbiology, 1978, vol. 35, No. 3 pages 618 to 621.

A11: Dallos and Hughes, British Journal of Ophthalmology, 1972, Vol. 56, pages 114 to 119.

V. Oral proceedings were held, attended by the Respondent, the Appellant having previously notified the Board that he was content for the case to be decided on his written submissions.

VI. At the end of the oral proceedings, the Respondent requested a patent be maintained on the basis of the further amended patent specification submitted at the oral proceedings, of which Claim 1 differs from that set out in paragraph I above in that there is added at the end the words "and inactivate the proteolytic enzyme"

VII. The Appellant, in the notice of appeal and in the Statement of Grounds, requested that the decision under appeal be set aside and the patent revoked in its entirety.

VIII. The Appellant's argumentation may be summarised as follows:

At the priority date of the patent in suit it was well known to clean contact lenses using enzymes and also well known to disinfect such lenses by heat treatment. The patent in suit requires only that these two process steps, previously carried out consecutively,, are combined into a single step. It was further known at the priority date that there were optimum conditions, e.g. of temperature, for the activity of a particular enzyme; for those of mammalian origin the optimum temperature is usually around physiological temperature, whereas those

of plant or microbiological origin frequently have much higher optimum temperatures. There can be nothing inventive in establishing the optimum temperature for an enzyme and using it at that temperature.

From A1 is known that the enzyme papain is most effective in cleaning contact lenses at temperatures in the range of 60 to 70°C. Cleaning at 80°, although less effective than at 60°C, is superior to cleaning at 40°C. A1 therefore embraces enzyme cleaning of contact lenses at temperatures known, e.g. from B3, A10 and A11, to be disinfecting temperatures. Moreover the most effective temperature range of 60 to 70°C disclosed in A1 lies wholly within the preferred range of between 60°C and 85°C according to the patent in suit and largely overlaps the most preferred range of 65 to 75°C. The gradual increase in temperature required by Claim 1 is trivial, since conventional thermal disinfection devices invariably have a heating cycle involving gradual heating to the maximum temperature, as is in substance acknowledged in the patent in suit, page 4, lines 1 to 9.

The subject-matter of Claim 1 is therefore entirely predictable from the disclosure in A1 and the common general knowledge of the skilled person.
The Respondent argues that the disclosure in A1 adds nothing to what was previously known regarding the optimum temperatures for enzyme cleaning, therefore does not contribute, before the priority date of the patent in suit, a teaching removing a previously held prejudice. The industry had sought since the early 1970's a simpler, e.g. single-step process for cleaning contact lenses but had rejected simultaneous enzyme cleaning and heat disinfection because it was believed that denatured protein would deposit on the lens (B8, and also B1, B6, B7, B9, and A8).

Reasons for the decision

1. The appeal is admissible

2. The question of compliance with Article 123 EPC of Claim 1 as allowed by the Opposition Division was not in dispute (see paragraph 7 of the decision maintaining the patent in amended form) and the Board sees no reason to go into this question. Claim 1 now under consideration contains the additional feature that the heat treatment should be such that the proteolytic enzyme is inactivated. This finds a basis on page 2, lines 34, 35 and page 3, lines 60 to 62 of the published patent, and since there is a counterpart in the application documents, the requirements of Article 123 EPC are also met in this respect.

3. A1 is the nearest prior art document, because it discloses enzyme cleaning of contact lenses at temperatures (60-70°C and 80°C) falling within the range mentioned in Claim 1. A1 does not however disclose, even implicitly, a heating cycle as is required by Claim 1, whose subject-mater for this reason at least is therefore novel.

4. At the priority date of the patent in suit it was known, e.g. from B2 to clean contact lenses of proteinaceous material using a proteolytic enzyme in aqueous solution and to disinfect the thus cleaned lenses by a subsequent heat treatment. According to the patent in suit this method suffers from the disadvantage that it is time consuming, requiring up to 13 hours. This, coupled with the fact that two step are involved, leads to poor patient compliance. Accordingly, the problem which is the basis of the patent in suit can be seen as the

provision of a shorter, more convenient method of cleaning contact lenses than the above-mentioned two-step process, as is in effect stated on page 2, lines 24, 25 of the patent in suit.

5. No contribution to inventive step can be seen in the recognition of the problem, since it is not in dispute between the parties that the problem has been known to practitioners for some time. This is corroborated by B8 and B10, relating to evidence adduced in Opposition Proceedings on EP-B-0 219 220 (proprietor is the present Respondent), which include extracts from a transcript of the trial between Allergan and Alcon in a US District Court, indicating that one of the marketing needs in lens care has been, since the early 1970's a product which is simple to use in order to increase patient compliance.

6. The problem is solved according to the patent in suit by the features of the characterising portion of Claim 1, which in summary are that the enzyme cleaning and heat disinfecting are combined into a single step, the times and temperatures involved being further defined as being sufficient to clean and disinfect the lenses and to inactivate the proteolytic enzyme. The said further features are in the Board's opinion limitations which are sufficiently clear in the context of the patent in suit.

7. The question to be answered is therefore whether it was obvious at the priority date of the patent in suit to combine the two steps of the prior art process known e.g. from B2, into such a single step process.

8. In this respect it would appear to be agreed between the parties, and by the Opposition Division, that A1

represents the most pertinent prior art and the Board shares this view, (see paragraph 3 above).

9. A1 relates *inter alia* to the enzymatic removal of protein deposits from contact lenses and on pages 1133 and 1134 there is described an experiment wherein a lens is divided into four pieces, of which three were treated with the enzyme papain for 30 minutes at 40°C, 60°C and 80°C. It was found that treatment at 60°C was most effective, a trace of deposit remaining on the piece treated at 80°C (page 1133, right column). A1 goes on to say that the effectiveness of the papain solution rapidly decreases when the temperature reaches 80°C or above, and in the summary on page 1135 concludes that the most effective temperature falls between 60°C and 70°C.

10. As indicated in paragraphs 3 and 9 above, A1 therefore teaches enzymatic cleaning of contact lenses at temperatures falling within the range specified in Claim 1. Moreover the said range embraces temperatures known to be disinfecting temperatures from A10 (75°C to 80°C), A11 (70°C) and B3 (80°C). However A1 contains no indication that the thus treated lens portions were sterile, let alone that a thus treated lens would not only be sterile but ready for reinserting onto the eye (cf. the patent in suit, page 3, lines 64 and 65). Moreover the wording in A1, page 1133, left column can only be interpreted as disclosing that the lens portions were introduced into the enzyme solution at the treatment temperature and not submitted to the heating cycle required by Claim 1. Moreover the sentence bridging pages 1132 and 1133 states that lenses should be thoroughly rinsed well prior to sterilising by boiling, so that from A1 as a whole it can only be derived that enzyme treatment, even at elevated

temperature, has to be following by rinsing and heat-treatment for disinfection.

11. The other documents cited by the Appellant, (series A) are less pertinent for the following reasons:

A2 discloses that enzyme cleaning of contact lenses using protease at 30°C is enhanced by use of a wetting agent, i.e. no suggestion of subject-matter of Claim 1. A3 discloses that enzyme cleaning of contact lenses is best at 37°C and diminished at 47°C therefore leading away from use of higher temperatures.

According to A4 enzyme treatment at 40°C is no better than at 25°C and at 43°C is inferior.

A5 teaches merely that treatment at 37°C is better than at room temperature.

A6 does not relate to contact lenses, but to the heat stability of the enzyme papain. A6 confirms that the optimum temperature for papain is 65 to 70°C. It is denatured on heating in solution at 82 to 83°C, but can withstand high temperatures for a time in the dry state.

A7 discloses that the optimium activity of proteases is at 50°C, and except at pH6 decreases from 50 to 60°C. A8 discloses compositions for cleaning contact lenses and contains examples of treatment at temperatures up to 100°C. In the case however of compositions containing enzymes, treatment is at room temperature.

Finally A9, a review article on proteinases but not relating to contact lens cleaning, discloses that the optimum temperature for the enzyme subtilison is in the region of 50 to 60°C and that it retains some activity at 70°C (pages 62 to 64) and further that the optimum

temperature of the enzyme esperase is similar (pages 68 and 69).
None of these documents, or A10 or A11, contains any teaching which when combined with that of would lead the average skilled person in the direction of the subject-matter of Claim 1. The various disclosures relating to the optimum temperatures for proteolytic enzymes show rather that A1 was saying nothing new in this respect, it having been known since as long ago as 1957 (A6) that certain enzymes had an optimum activity at elevated temperatures, corroborated moreover by B4 and B5, disclosing in 1971 that the optimum temperature for proteases is 57 to 67°C.

12. On the other hand it is apparent from the documents cited by the Respondent (series B) that those skilled in the art at least had reservations about heating contact lenses at disinfecting temperatures in the presence of protein, whether it was the protein contaminating the lens or the enzyme which was being used to remove it. In particular, B1, page 388, left column, warns that it is most important ... to well rinse the lens prior to boiling. If this is not done, residual enzyme, being proteinaceous, will be re-bound to the lens. The middle column goes on to indicate that problems with protein films are worse with thermal disinfection. Moreover B7, at page 163, states that whatever the cleaning technique, heat is not recommended because of the risk of protein coagulation, demonstrating that a prejudice still existed in 1987, some four years after the priority date of the patent in suit.

13. It was therefore not obvious at the said priority date to combine the two known cleaning and disinfecting steps into the single step process as defined in Claim 1, and in particular surprising that at the end of the said process, the lens is ready for insertion onto the eye.

Cleaning and disinfecting is complete in about 1 hour, thereby meeting the object of the patent to provide a simple and less time-consuming regimen and thus enhance patient compliance. The Board notes moreover that a lens care regimen based on the patent in suit is commercially available and has obtained FDA approval.

14. It is true, as argued by the Appellant, that conventional thermal disinfection involves a heating cycle in which the temperature is gradually raised to the disinfecting temperature, and this corresponds closely to the heating cycle required by Claim 1. However none of the documents relating to enzyme cleaning at elevated temperature disclose such a temperature cycle, let alone that it should be such as to clean and disinfect the lenses and also to inactivate the proteolytic enzyme.

15. The subject-matter of Claim 1 is therefore seen as involving an inventive step in the sense of Article 56 EPC. Claim 1 is thus allowable (Article 52(1) EPC).

16. Since the whole patent as amended meets the requirements of the convention, it can be maintained in this amended from (Article 102(3) EPC).

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to grant a patent on the basis of the amended patent document as filed at the oral proceedings.

The Registrar: The Chairman:

P. Martorana E. Turrini