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D E C I S I O N
of 29 January 2003

Case Number: T 0699/98 - 3.3.7

Application Number: 88301108.2

Publication Number: 0278744

IPC: A61K 7/16

Language of the proceedings: EN

Title of invention:

Dentifrice composition for desensitising sensitive teeth

Patentee:

UNILEVER PLC, et al

Opponents:

01 SmithKline Beecham plc
03 Colgate-Palmolive Company

Headword:

-

Relevant legal provisions:

EPC Art. 54, 56, 69, 83, 84, 123(2)(3)
EPC R. 27(1)(b)

Keyword:

"Novelty (yes) - combination of disclosures"
"Inventive step (yes) closest prior art - problem and solution"
"Amendments (yes) - deletion of an alternative feature"
"Amendments (yes) - deletion of the term "synergistic" added to the description as granted"
"Claims - interpretation - clarity (yes)"

Decisions cited:

T 0219/83, T 0010/97

Catchword:

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Case Number: T 0699/98 - 3.3.7

D E C I S I O N
of the Technical Board of Appeal 3.3.7
of 29 January 2003

Appellant:
(Opponent 03)

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Decision under appeal:

**Interlocutory decision of the Opposition Division
of the European Patent Office posted 22 May 1998
concerning maintenance of European patent
No. 0 278 744 in amended form.**

Composition of the Board:

Chairman: R. E. Teschemacher
Members: B. J. M. Struif
P. A. Gryczka

Summary of Facts and Submissions

- I. European patent No. 0 278 744 with respect to European patent application No. 88 301 108.2, filed on 10 February 1988, was granted on the basis of five claims, claim 1 reading as follows.

"A dentifrice composition for desensitising sensitive teeth, characterised in that it comprises in combination a water-soluble source of potassium ions selected from the group consisting of potassium nitrate, potassium citrate, and potassium bicarbonate, and 2,4,4'-trichloro-2'-hydroxy-diphenyl ether, together with usual dentifrice ingredients."

Claims 2 to 5 were dependent on claim 1.

- II. Three notices of opposition were filed against the granted patent, in which the revocation of the patent in its entirety was requested on the grounds of Article 100(a) EPC with respect to lack of novelty and inventive step and on the grounds of Article 100(b) EPC with respect to insufficiency of disclosure. During the proceedings before the opposition division *inter alia* the following documents were considered:

D1: EP-A-0 161 898

D2: EP-A-0 095 871

D3: Journal of Clinical Periodontology, vol. 10, 1983, p. 351-363

D12: Abstract 703 of Journal of Dental Research, 1994, V. Kjaerheim et al., "Effect of Triclosan on neuromuscular transmission in the Rat"

In addition, the patentee and opponents 02 and 03 submitted the following test reports:

D13: Patentee's test report

D14: Declaration of N. Nabi

D15: Declaration of M. Williams

D16: Declaration of K. Markowitz

By letter dated 5 November 1996, opponent 02 withdrew its opposition.

III. In a decision of the opposition division issued in writing on 22 May 1998, the patent was maintained in amended form. That decision was based on a set of claims 1 to 4 as the sole request. Claim 1 read as follows:

"A dentifrice composition for desensitising sensitive teeth, characterised in that it comprises in combination **0.7 % to 3 % (calculated as potassium) by weight of the dentifrice composition of** a water-soluble source of potassium ions selected from the group consisting of potassium nitrate, potassium citrate, and potassium bicarbonate, and 2,4,4'-trichloro-2'-hydroxy-diphenyl ether, together with usual dentifrice ingredients." (emphasis added on the differences from claim 1 as granted). In the following the compound "2,4,4'-trichloro-2'-hydroxy-diphenyl ether" is named "Triclosan".

Claims 2 and 3 as granted remained unamended. After cancelling granted claim 4, claim 5 as granted was renumbered as claim 4.

The decision was based in essence on the following reasons:

- (a) The amended claims and the amendments to the description including the cancellation of the term "synergistic" were considered to meet the requirements of Articles 123(2) and (3) EPC.
- (b) As regards sufficiency of disclosure, the patent in suit clearly disclosed how to prepare a dentifrice as claimed.
- (c) The subject-matter of amended claim 1 was novel.
- (d) As regards inventive step, D2 was considered to be the closest state of the art. The problem underlying the patent in suit was to provide a dentifrice composition for desensitising sensitive teeth. The patentee's test data showed that the combined use of potassium citrate and Triclosan provided an improved analgetic effect. The Markowitz test results were based on a simple in-vitro diffusion test and were therefore not convincing. The Nabi tests lacked a control test without potassium nitrate. The Williams tests contained the polymer Gantrez S-97 and were prone to placebo effects.

Neither D1, which concerned a different problem nor any of the other cited prior art documents suggested the combination of Triclosan with the specified potassium salts for providing the specific technical effect, so that the claimed subject-matter also involved an inventive step.

IV. On 17 July 1998 the opponent 01 filed a notice of appeal against the above decision, the prescribed fee being paid on the same day. On 10 July 1998 the

opponent 03 filed a notice of appeal against the above decision, the prescribed fee being paid on the same day. The statements setting out the grounds of appeal were filed on 17 September 1998 and 29 September 1998, respectively.

- V. By letter dated 8 February 1999, the respondent (patentee) filed two auxiliary requests and submitted the following post-published document:

D17: EP-A-0 696 450

- VI. In a communication dated 31 October 2002, the board addressed the points to be discussed during the oral proceedings.

- VII. By letter dated 20 November 2002, opponent 01 withdrew its opposition.

- VIII. The opponent 03 (in the following named "appellant") argued in substance as follows:

(a) Granted claim 1 contained added subject-matter in view of the restriction to three selected potassium salts. Since the application as originally filed referred to four different salts and no preference to the claimed three potassium salts was originally disclosed the amendment violated Article 123(2) EPC.

(b) No synergistic effect could be deduced from the application as filed. The deletion of the term "synergistic", which was added to the patent as granted in the examination procedure violated the requirements of Article 123(3) EPC.

Furthermore, the claims on file had to be interpreted in the light of the description under Article 69 EPC and were limited to those combinations which showed a synergistic effect. By cancellation of that term, the scope of protection could now be interpreted more broadly than if that term was present.

- (c) As regards clarity, the term "synergistic" represented an essential technical feature of the patent in suit and its deletion contravened Article 84 EPC.
- (d) As regards insufficiency of disclosure, Triclosan was a substantially water-insoluble antibacterial agent, which could not pass the tubular orifices within the dentin to reach the intradental nerves. The patent in suit did not disclose all features necessary for making insoluble Triclosan bioavailable to the nerves, in order to provide a beneficial technical effect.
- (e) The claimed subject-matter lacked novelty, since all features of amended claim 1 could directly and unambiguously be derived from D1, example 5, table VI in combination with example 2, table II, column C and page 9, lines 17 to 23. The amount of the potassium salt could be calculated easily.
- (f) As regards inventive step, D1 represented a proper starting point for the problem-solution approach. There was no difference between the purpose aimed at in the patent in suit and that of D1 since the known dentifrice was also suitable for desensitising sensitive teeth. Since the only difference from D1 was the claimed amount of potassium and no improved effect had been shown for that difference, the problem to be solved over

D1 was the provision of a mere alternative. Even if the problem over D1 was seen in providing a dentifrice having an improved antiplaque activity the claimed solution was also made obvious by D1.

Starting from D2 as the closest prior art document, the claimed subject-matter differed therefrom by the presence of Triclosan which was a known antiplaque agent. The problem to be solved over D2 was seen in the provision of a suitable antiplaque agent for the dentifrice. Since it had not been shown that Triclosan had any desensitising effect on sensitive teeth, the claimed dentifrice was obvious over the combination of D2 with D1.

No unexpected synergistic effect had been shown for the claimed combination. The respondent's tests reported in D13 were carried out with aqueous solutions and not with dentifrices and furthermore by using isolated spinal nerve roots, which conditions could not be compared with those of an oral cavity. The measured desensitising effect could be attributed to ethanol added to the test solutions. Furthermore, the tests did not use the claimed amount of water-soluble potassium. The Nabi and Markowitz experiments showed that Triclosan would neither reach the nerve ends nor could have any synergistic desensitising effect in combination with potassium salts. The Williams in-vivo tests showed that the claimed combination did not provide any advantages compared with a dentifrice only comprising a potassium salt.

Although D17 described after the filing date of the patent in suit that Triclosan had a desensitising effect, the teaching thereof was quite different from the claimed subject-matter.

Consequently, the claimed subject-matter did not involve an inventive step.

IX. The arguments of the respondent can be summarized as follows:

- (a) Regarding Article 123(2) EPC, the application as originally filed disclosed four different potassium salts from which one alternative had been cancelled. This deletion did not amount to added subject-matter.
- (b) The term "synergistic" could be derived from the application as filed page 2, lines 29 to 33 and was introduced in the description when discussing the advantages vis-à-vis the cited prior art. Thus, the deletion of this term in the patent in suit did not contravene the requirements of Article 123(3) EPC.
- (c) The claims were clear and concise.
- (d) The patent in suit disclosed dentifrice compositions, in particular in the examples, in a sufficiently clear manner for the skilled person to reproduce them.
- (e) As to novelty, D1 did not directly and unambiguously disclose the claimed combination of ingredients of the claimed dentifrice. By the presence of only slightly water-soluble zinc citrate in the examples of D1, the claimed amount of citrate ions could not be reached.

f) Regarding inventive step, D2 could be considered as the nearest prior art document, since it was focused on desensitising sensitive teeth. D1 did not represent a proper starting point for the problem-solution approach, since it concerned dentifrices having an antiplaque effect. There was no indication in D1 that Triclosan would provide a desensitising action on sensitive teeth. The problem to be solved over D2 was seen in providing a dentifrice having an improved desensitising effect. The respondent's test report (D13) showed that the claimed combination provided a surprising reduction in nerve sensitivity. The analgetic effect of Triclosan had been shown in the post-published literature D12 and D17.

The appellant's tests were deficient. The Nabi and Markowitz tests (D14 and D16) used a model which was not comparable to a real tooth environment. The Williams tests (D15) lacked a control and were prone to placebo effects. Furthermore, the compositions A and B tested therein differed considerably and did not allow to reach any reasonable conclusion.

Hence, the claimed subject-matter involved an inventive step.

X. The appellant (opponent 03) requested that the decision be set aside and that the patent be revoked.

XI. The respondent requested that the appeal be dismissed, and that the patent be maintained in the version underlying the decision under appeal. As an alternative he requested that the patent be maintained on the basis of one of the sets of claims submitted as first and secondary auxiliary requests with the letter dated 8 February 1999.

Reasons for the Decision

1. The appeal is admissible

Amendments

2. The appellant argued that the amendment to three selected potassium salts in claim 1 as granted was not supported by the application as originally filed (Articles 100(c) and 123(2) EPC).
 - 2.1 According to that amendment the water-soluble source of potassium ions is selected from the group consisting of **potassium nitrate, potassium citrate, and potassium bicarbonate** (emphasis added by the board). In the application as filed (claim 2 and page 2, lines 14 to 16) the above mentioned group additionally included potassium chloride as a further possible potassium salt. Since each of the four potassium salts is used in original examples 1 to 4 and is equally effective to reduce the sensitivity of hypersensitive areas of teeth (page 3, lines 44 to 46), there is no indication in the application as filed of any preference within this group of four compounds.
 - 2.2 Consequently, the deletion of potassium chloride from that list of individualised equally useful compounds is admissible (compare T 10/97 of 7 October 1999, cited in Case Law of the Boards of Appeal of the European Patent Office, 4th edition 2001, III.A.1.2, last paragraph). Hence, the requirements of Article 123(2) EPC are met.
3. The appellant argued that the deletion of the term "synergistic" from the patent specification violated the requirements of Article 123(3) EPC.

- 3.1 The term "synergistic" was introduced during examination procedure when citing D1 and D3 in accordance with Rule 27(1) b) EPC in the description (communication dated 29 June 1991, point 4(a); patent as granted, page 2, lines 29 to 39). In view of the results of tests provided during the examination procedure (D13), the following reference was added to the patent specification: "They (**documents D1 and D3**) did not suggest any treatment with a combination of certain potassium salts and Triclosan, which according to the present invention was surprisingly found to produce an unexpected, **synergistic** desensitising effect." (addition by the board).
- 3.2 The question, whether in the amended context, the term "synergistic" comprises added subject-matter which goes beyond the application as originally filed under Article 123(2) EPC can be left unanswered, since that term has now been deleted from the description.
- 3.3 According to Article 123(3) EPC the claims of the European patent may not be amended during opposition proceedings in such a way as to extend the protection conferred. The amendments to the claims during opposition proceedings concern only the addition of the amount of the water-soluble source of potassium ions (calculated as potassium). That amendment which has not been objected to, restricts in fact the scope of protection. The deletion of the term "synergistic" concerns an amendment of the description but not of the claims and is thus not in itself objectionable under Article 123(3) EPC.
4. The appellant argued however, that the claims would be interpreted more narrowly on the basis of the description of the patent as granted which contained a reference to a "synergistic effect".

- 4.1 According to Article 69 EPC the extent of protection conferred by the European patent shall be determined by the terms of the claims. Nevertheless, the description shall be used to interpret the claims.
- 4.2 The granted and amended claims are directed to a dentifrice composition for desensitising sensitive teeth in the form of product claims. Such a claim category confers the broadest and also unconditional protection for dentifrice compositions which are suitable for desensitising teeth. There is no dispute between the parties that the claimed compositions show a desensitising effect. Consequently, the scope of protection of such product claims is independent of how that technical effect is explained in the description of the patent in suit in comparison to the state of the art. In any case, the appellant's interpretation is not in conformity with the description as a whole, because the preceding paragraph in the description dealing in general with the effects of the two components states, that "the dentifrice of the invention has a two-pronged attack on the problem of sensitive teeth. The **independent actions** of its two active components result in the product of the invention having a surprising degree of effectiveness which cannot be attained by the use of either component alone" (page 2, lines 24 to 26, emphasis added). This passage makes clear that the invention as described is not restricted to embodiments showing a synergistic **interaction** of its active components. Hence, the deletion of the term "synergistic" in the patent specification has no effect on the extent of protection under Article 69 EPC.

Clarity

5. The appellant furthermore argued that the deletion of the term "synergistic" in the description contravened Article 84 EPC.

5.1 According to Article 84 EPC, the claims shall define the matter for which protection is sought. They shall be clear and concise and be supported by the description. Since clarity is not an opposition ground, only amendments to the granted claims are open to objections under Article 84 EPC. However, the appellant has not raised any clarity objection to the amendments made in the claims. Consequently, the only question, which may arise with respect to the term "synergistic" is, whether its deletion from the description has introduced any inconsistency between the claims and the description, which need, if necessary, interpretation.

5.2 The essential technical features of the claimed dentifrice are specific chemically defined compounds, namely Triclosan and specified water-soluble potassium salts in specific amounts with the proviso that the composition is suitable for desensitising sensitive teeth. The appellant has not provided any argument as to which way these technical features of the claims should be unclear or provide inconsistent or contradictory information which need interpretation by the description. Also the board sees no clarity objections in this respect.

Since the definition of the claimed dentifrice is clear and concise and does not need interpretation by the description and since the deletion of the term "synergistic" from the description does not obscure the claims, that amendment cannot contravene the requirements of Article 84 EPC.

Sufficiency of disclosure

6. According to Article 83 EPC, the European patent application must disclose the invention in a manner sufficiently clear and complete for it to be carried out by the skilled person. The essence of the appellant's argument regarding lack of disclosure is that the dentifrice could not be reproduced because Triclosan was substantially water-insoluble and that the patent in suit did not disclose how the insoluble Triclosan was made bioavailable to the nerves by the claimed dentifrice.

6.1 The claimed subject-matter concerns a dentifrice comprising two main components one of which is Triclosan. This component is a commercial product known to be water-insoluble. The question which arises under Article 83 is whether the claimed dentifrice can be formulated by the person skilled in the art by using the guidance of the patent in suit and common technical knowledge. The patent in suit not only specifies the essential components of the dentifrice and their amounts in the composition (claim 1 and 4 as amended) but also indicates the typical ingredients known to those skilled in the art (page 2, lines 43 to 46). A specific reference is made to polyethylene glycol for use in toothpastes containing Triclosan (page 2, lines 47 to 51). Furthermore, in the examples of the amended patent specification four dentifrice compositions are disclosed comprising Triclosan together with potassium salts and other ingredients including polyethylene glycol. The compositions are said to be effective to reduce the sensitivity of hypersensitive areas of the teeth, especially that of the tooth dentine (patent in suit page 44 to 46).

- 6.2 Consequently, that disclosure enables the person skilled in the art to formulate dentifrices within the ambit of the claims. Since the skilled person knows that Triclosan is water-insoluble, he is able to use suitable ingredients, such as polyethylene glycol in the dentifrice composition, to render the Triclosan bioavailable and to make, if necessary, some orienting tests in this respect.
- 6.3 Furthermore, the appellant has not submitted any evidence for his allegation that the claimed dentifrice cannot be reproduced according to the guidance of the patent specification. The onus of proof in this respect lies, however, with the opponent (appellant) (T 219/83, OJ EPO 1986, 211). This, the appellant has failed to discharge.
- 6.4 Consequently, the board is satisfied that the invention is clearly and sufficiently disclosed for it to be carried out by the skilled person within the whole ambit of the claims, so that the requirements of Article 83 EPC are met.

Novelty

7. The Appellant argued that all features of amended claim 1 could directly and unambiguously be derived from D1, example 5, table VI in combination with example 2, table II, column C and page 9, lines 17 to 23.
- 7.1 D1 discloses a dentifrice composition effective to inhibit the growth of dental plaque comprising a surfactant and an anti-plaque agent consisting of a substantially water-insoluble non-cationic antimicrobial agent or a zinc salt having a water solubility greater than 2×10^{-4} g per 100 g of water at 25°C and at pH 7, or a mixture thereof, characterized

in that there is present a lamellar liquid crystal surfactant phase having a lamellar spacing of less than 6.0 nm in an amount of at least 0.2% by weight of the dentifrice composition (claim 1). The composition may further include 0.1 to 3% by weight of sodium chloride or a water-soluble salt, other than a fluorine-containing salt, in an equivalent molar cation concentration (claim 4). As antimicrobial agent phenolic and bisphenolic compounds, halogenated diphenyl ethers, benzoate esters and carbanilides are mentioned (page 11, line 4 to page 12, line 28). Preferred antimicrobial agents are halogenated bisphenolic compounds and halogenated hydroxydiphenyl ethers, in particular Triclosan and 2,2'-methylene bis(4-chloro-6-bromophenol) (page 12, lines 32 to 35, claim 7). The cation of the added salt may be sodium, potassium, aluminium, magnesium or zinc, preferably, sodium and aluminium and suitable anions are acetate, chloride, citrate, gluconate, lactate, sulphate, phosphate, tartrate, glyconate and ascorbate (page 9, lines 10 to 16).

- 7.2 Example 2 describes a toothpaste which contains *inter alia* 0.5% by weight of zinc citrate trihydrate, 0.2% by weight of Triclosan and 0.5% by weight of sodium chloride (page 20, table II, composition C). A series of toothpastes was made having the ingredients of toothpaste C of example 2, the sodium chloride however being replaced by another salt in an amount which is equivalent to the same molar cation concentration as 0.5% sodium chloride (example 5, page 23, lines 30 to 33, table VI, page 24, and lines 24 to 26). These compositions include potassium salts in an amount of 0.34% by weight of the dentifrice (when calculated as potassium). The mentioned potassium salts are potassium chloride, lactate, tartrate, gluconate and acetate, none of which is claimed.

7.2.1 The appellant argued that the composition in example 5 of D1 also contained zinc citrate and provided a source of citrate ions. This would result in an aqueous solution containing Triclosan, potassium ions and citrate ions.

7.2.2 However, the amount of potassium in all five samples of table VI is 0.34% by weight and is thus lower than the claimed amount of 0.7 to 3.0% by weight and hence provides a distinction over the exemplified compositions of D1. Consequently, the question can be left unanswered, whether the amount of water-soluble citrate, which may be present in view of the presence of 0.5% by weight of sparingly water-soluble zinc citrate trihydrate, meets the requirements of the claimed composition.

7.3. The appellant's argument that the claimed subject-matter could be derived from compositions disclosed in table VI when read in connection with the general description is not convincing.

7.3.1 The claimed dentifrice specifies the kind and amount of the potassium salts and the kind of the anti-microbial agent (Triclosan) and thus comprises at least three variable features in specific combination. Although in D1 Triclosan is used as antibacterial agent, examples 3 and 4 disclose eleven embodiments which use a type of antimicrobial agent other than Triclosan. Furthermore, table VI discloses fifteen individual compositions including fifteen different salts, only five of which are potassium salts. However, the preferred salts are those of sodium and aluminium (page 9, lines 14 and 15).

7.3.2 Furthermore, the water-soluble potassium salts mentioned in table VI are not potassium nitrate, citrate or bicarbonate as claimed. Other suitable

anions are mentioned within a list comprising ten different anion types (point 7.1; page 9, lines 10 to 13). Finally, the claimed amount of such water-soluble potassium salts is to provide 0.7 to 3% by weight (calculated as potassium) of the dentifrice. In D1 the general range used for the amount of the electrolyte source is 0.1 to 3% by weight referred to sodium chloride (page 9, lines 18 to 21) and does not allow without hindsight a direct conclusion to the claimed range calculated as potassium.

- 7.4 From the above it follows that the composition as claimed is considered as the result of a "multiple selection" within the disclosure of D1. There is no pointer in D1 to the particular combination of features as claimed. It is not sufficient to destroy novelty of such a combination, to associate with the knowledge of the invention, the ingredients selected from different possibilities which may be offered by the prior art document so as to create in an artificial way a composition of the patent in suit. Quite to the contrary, the claimed combination must directly and unambiguously be derivable from this document. Since D1 does not disclose such a composition, the claimed subject-matter is novel.

Closest prior art document

8. The patent in suit concerns a dentifrice composition for desensitising sensitive teeth.
- 8.1 Dentifrice compositions are known from the prior art, in particular D1, which the appellant regarded as the closest prior art document and from D2, which was the starting point for the opposition division and the respondent.

- 8.1.1 D1 aims at a dentifrice composition comprising a water-insoluble non-cationic antimicrobial and a lamellar liquid crystal surfactant phase having a specific lamellar spacing which is able to deliver the antimicrobial agent to the tooth surface, where it is retained for a time sufficient to materially affect the rate of plaque regrowth, the rate of plaque metabolism and the equilibrium plaque level (page 2 and 3 bridging paragraph; point 7.1 above). A decrease in lamellar spacing of the liquid crystal surfactant phase increases the effectiveness of the toothpaste in inhibiting plaque (table I, page 19).
- 8.1.2 D2 describes a tooth treatment composition in liquid or paste form, to counter tooth hypersensitivity, comprising potassium and citrate ions in an antihypersensitivity effective amount (claim 1). The potassium and citrate ions present expressed as $K_nH_{3-n}C_6H_5O_7$, wherein $n = 1, 2$ or 3 , amount to up to 40%, preferred up to 10%, and in particular from 0.3 to 9% by weight of the total composition (claims 5 to 7). Tooth sensitivity is exhibited when a sufferer experiences a painful reaction to *inter alia* pressure, hot, cool, sweet and the like stimuli of the tooth surface (page 1, lines 4 to 9). According to D2, known compositions for reducing hypersensitivity include protein precipitants, for example formalin, silver nitrate, strontium chloride or phenol, or tubule occluding agents such as certain fluorides, calcium hydroxide, calcium phosphate, nitrates of alkali metals, especially potassium nitrate, strontium chloride and also silver nitrate and formalin (page 2, lines 7 to 13). These desensitising components are said to have an unpleasant salt flavour, which is difficult to mask rendering compositions containing them more or less unpleasant to use.

Thus, the teaching of D2 is directed to a composition comprising potassium citrate ions for efficacious treatment of tooth hypersensitivity, without the above-stated disadvantages (page 2, line 25 to page 3, line 8).

- 8.2 According to the patent in suit, dental plaque is the major cause of oral disease. Plaque acids attack the tooth enamel leading to caries, and toxins produced by the plaque cause inflammation of the gums (gingivitis) and eventually gum recession and tooth loss (parodontitis). Recession of the gum from the tooth exposes the dentin of the root, which can therefore be damaged making the tooth sensitive to tactile and/or thermal stimuli. The resultant pain can make toothbrushing uncomfortable thus leading to inefficient plaque removal and further exacerbation of the problem (page 2, lines 4 to 9).

Potassium salts, such as potassium nitrate, potassium citrate, or potassium bicarbonate, are known as tooth desensitising agents and are considered to be effective to reduce the pain associated with sensitive teeth. They act, as do other water-soluble potassium salts which produce potassium ions, directly on exposed tooth dentin (page 2, lines 17 to 22).

- 8.3 The patent in suit aims at providing a dentifrice comprising a combination of ingredients, which mitigates the problem of sensitive teeth and provides superior effectiveness (claim 1 and page 2, lines 10 to 12).

- 8.4 According to established case law, the closest prior art for the purpose of assessing inventive step is that which corresponds to a purpose or technical effect similar to the invention requiring the minimum of

structural and functional modifications (Case Law of the Boards of Appeal of the European Patent Office, 4th edition 2001, I.D.3.1).

- 8.5 As can be seen from the above, D2 refers to the ability of preventing and remedying dentinal hypersensitivity by using potassium citrate as desensibilising agent, whilst D1 relates to the inhibition of dentinal plaque growth. Although D1 mentions Triclosan as antimicrobial agent and different salts *inter alia* potassium salts as electrolyte source to control the specific layer spacing, there is no indication in D1 that these dentifrices could have the purpose of desensitising sensitive teeth or should be used in this respect. Since D2 is more closely related to the technical purpose and effect aimed at in the patent in suit than D1, D2 is the most appropriate starting point.

Problem and solution

- 9.1 According to the examples of the patent in suit the compositions are effective to reduce the sensitivity of hypersensitive areas of the teeth, especially that of the tooth dentine (patent in suit page 3, 44 to 46). In order to show experimental evidence for an improvement over dentifrice compositions of D2 the respondent has referred to his test report D13.
- 9.2 In those in-vitro tests, spinal nerve roots of the cauda equina isolated from fresh killed rats are placed between stimulating and recording electrodes in a nerve bath similar to that developed by Orchardson (1974). Compound nerve action potentials (CAPs) evoked by electrical stimulation of the nerve bundles are recorded and measured as peak CAP amplitude (A-CAP) and as the area under the waveform (I-CAP) at 30 second intervals. By using that in vitro model, potassium citrate, Triclosan and a mixture of potassium citrate

and Triclosan in Krebs solutions were tested in comparison to a solution without said ingredients as control. To assist Triclosan solubility, all solutions also contained 1% ethanol (D13, page 1, last paragraph). The measured reductions in nerve conduction are expressed as percentage based on 100% for a control sample (table, page 2). The lower the percentage the better is the effect. It can be seen from the results that both potassium citrate (76 and 85%) and Triclosan (90 and 92%), when used separately, are effective in reducing the nerve conduction. The measured values for the combined use are 52% and 54%, respectively and demonstrate a considerably improved effect compared to potassium citrate, when used alone. These results surpass the purely additive effect which may be predicted from the expected reduction for the combined use ($76\% \times 90\% = 68\%$ and $85\% \times 92\% = 78\%$, respectively) and thus show even a synergistic effect for those tests.

9.3 The appellant objected to the above in-vitro tests because they used on the one hand simple aqueous solutions but no dentifrices and on the other hand isolated spinal nerve roots quite different from an oral cavity so that the tests did not demonstrate any direct therapeutic desensitising effect on sensitive teeth. Further, the solution contained ethanol which might have a desensitising effect as well.

9.3.1 It is difficult to directly demonstrate therapeutic desensitivity on teeth by in-vivo tests due to the well known placebo effect described by toothpaste studies in the literature (D3, page 358, right column, summary and 359, point 3). Thus, the respondent's test has been developed as an in-vitro model for assessing intradental nerve excitability by using rat spinal nerves which has been considered as suitable in the literature for the evaluation of nerve activity in

sensitive teeth (see D13, introduction, second paragraph). Consequently, it appears that such in-vitro tests are suitable for the evaluation of the desensitising effect on teeth.

9.3.2 It is evident that in such in-vitro model tests neither the conditions of the oral cavity can be exactly simulated nor can a dentifrice be used. It is thus quite reasonable to use an artificial extracellular fluid and an amount of potassium salt which might correspond to that which actually may reach the intradental nerve ends. That the fluid contains 1% of ethanol to assist the Triclosan solubility is no hindrance to disregard the tests. In this respect, it is noted that all test solutions include 1% ethanol so that even if ethanol had, as argued, an additional effect on the nerve conduction, this effect would also be present in all other tests including the control.

9.3.3 Consequently, the appellant has not shown that the respondent's test report is unreliable and cannot be used to demonstrate an improved desensitising effect.

9.4 On the other hand, the appellant has relied on counter experiments, reported in the Nabi (D14), Markowitz (D16) and Williams (D15) test reports, to show that the claimed combination provides no improvement, in particular no synergism.

9.4.1 In the Nabi test report (D14) the bioavailability of Triclosan has been investigated by an in-vitro test, in which hydroxyapatite disks are treated with a dentifrice containing both Triclosan and potassium nitrate (composition A) or for comparative purpose with a similar dentifrice without potassium nitrate (composition B). The delivery and retention of Triclosan on the disks are determined to be 1.19 µg/Disk (composition A) and 63.39 µg/Disk

(composition B; tables I and II). A similar trend is observed when using commercial toothpastes (page 5, table III).

From those tests the appellant concluded that the bioavailability of the Triclosan on the disks is substantially inhibited by the presence of potassium nitrate.

Although the occlusion of dentinal tubes is regarded to be of prime importance to desensitisation and the uptake onto or into the dentine surface is considered to be necessary (D3, page 359, conclusion, point 2), the Nabi test results cannot be compared with those of D13 since they are based on completely different in-vitro models. Whilst D14 evaluates the bioavailability of Triclosan, D13 is based on measuring the nerve conduction. Furthermore, although the detected amount of Triclosan in the combined use is low, this result does not demonstrate that such an amount would be ineffective.

- 9.4.2 In the Markowitz test report (D16) the permeability of a 1 mm thick dentin disk (EDTA etched) was tested with a slurry of a dentrifice and saline by brushing said slurry onto the surface with a soft nylon brush for 4 minutes. The dentifrice contained 5.35% by weight of potassium citrate monohydrate and 0.3% by weight of Triclosan. The material which passed through the disk is analysed and shows 47 ppm potassium ion but no Triclosan.

Although the Markowitz tests appear to show that in such a model Triclosan does not penetrate through the dentin disk having a certain thickness, such an experiment has no bearing on the question whether the claimed combination has an improved desensitising effect on sensitive teeth or not. Furthermore, the

Markowitz tests are completely different from the patentee's tests and do not allow any comparison therewith, and still less a conclusion, in which way the respondent's tests could be unreliable.

- 9.4.3 In the Williams' in-vivo test report (D15) dentifrice compositions containing inter alia 5% by weight of potassium nitrate and 0.3% by weight of Triclosan (composition A) and a dentifrice composition containing only 5% by weight of potassium nitrate (composition B) have been tested in a four and eight week clinical study on fifty subjects (page 4, table I and page 5, table II). The results show that both compositions are effective in reducing existing dentinal hypersensitivity for different stimuli in a statistical significant manner after 4 and 8 weeks (tables III to VI).

The appellant concluded that statistically composition A is not more effective than composition B after 4 and 8 weeks.

However, the compositions A and B not only differ in the presence and absence of Triclosan but also in the presence and the absence of other components. For example composition B contains Viscasin and polyethylene glycol which composition A comprising Triclosan, does not contain. Polyethylene glycol is, however, specifically mentioned in the patent in suit in relation to toothpastes containing Triclosan (page 2, lines 47 to 51) and is also used in the examples.

Furthermore, no tests which include a placebo dentifrice without both Triclosan and potassium nitrate have been carried out so that according to D3 the test results may be based on considerable placebo effects.

Finally, a precise analysis of the test data, in particular, tables III and IV, show at least with respect to a pain score after 4 weeks, a considerable improvement in sensitivity when using 10°C water (0.73 compared to 0.44) or tactile treshhold (15.67 compared to 6.26).

Consequently, although the Williams' tests are not comparable to the respondent's test, they nevertheless show a trend to a better desensitising effect when the claimed combination is used and are therefore not in contradiction to the respondent's test.

- 9.4.4 Documents published after the filing date of the patent in suit demonstrate that Triclosan has indeed an analgetic effect. In this respect reference is made to D12, published in 1994, which relates to the effects of Triclosan on the rat phrenic nerve diaphragma preparation (title). The authors have found that Triclosan which is added to toothpaste and mouthrinses in concentrations of as low as 10 ppm had a marked inhibitory effect on the neuromuscular transmission.

Furthermore, D17 published in 1996 discloses a two-component dentifrice for the treatment of hypersensitive teeth wherein a potassium salt is used as first desensitising agent in a first dentifrice component and Triclosan is used as a desensitising agent in a second dentifrice component wherein the components are maintained separately from each other until dispensed for application to teeth (claims 1, 2 and 4). Such two component dentifrices have an improved desensitising effect on the teeth as a result of the combined presence of both ingredients (page 3, lines 1 and 2).

- 9.5. From the above it follows that Triclosan has a desensitising effect on sensitive teeth on its own and that in this respect the respondent's test report D13 is in line with that finding and is thus more convincing than the test reports D14 to D16. Consequently, the board is satisfied by the evidence on file that the use of a dentifrice containing Triclosan in combination with specific potassium salts provides a more effective desensitising effect than the composition of D2.
- 9.6 Hence the problem to be solved over D2 may be seen in providing a dentifrice which has an improved desensitising effect on sensitive teeth in line with the patent in suit, page 2, lines 10 to 12 and page 3, lines 44 to 46.
- 9.7 According to the patent in suit, this problem is solved by a dentifrice composition comprising in addition to a water-soluble source of potassium ions
2,4,4'-trichloro-2'-hydroxy-diphenyl ether (Triclosan).

Obviousness

10. It remains to be decided whether the claimed subject-matter is obvious when starting from D2 and having regard to the other documents on file.
- 10.1 There is, in D2, neither a hint towards Triclosan nor any incentive to combine Triclosan with potassium citrate as claimed for improving the desensitising effect. Therefore, the claimed subject-matter is not rendered obvious by D2 alone.
- 10.2 The teaching of D1 specifically relates to a dentifrice composition effective to inhibit the growth of dental plaque but does not address the problem of preventing hypersensitivity of sensitive teeth. The salts added to

the dentifrice only have the function as electrolyte source to provide a sufficient electrolyte concentration in order to reduce the layer spacing of a surfactant liquid crystal phase to below 6 nm (page 8 and 9 bridging paragraph; table 1, page 20). There is no indication that Triclosan may be effective in desensitising hypersensitive teeth, in particular, when combined with a specified amount of potassium salts. There is no mention in D1 that the exemplified compositions containing potassium salts could have any desensitising effect or that they should be used for that purpose. Since the desensitising effect of Triclosan is not mentioned in D1, there is no incentive from D1 to modify the teaching of D2 in a direction as claimed by incorporating Triclosan into the dentifrice.

The other documents cited during the proceedings are not more relevant than those analysed above. In particular, they do not disclose any desensibilising effectiveness of Triclosan against sensitive teeth. Thus, the claimed subject-matter is considered to be inventive when taking D2 as the starting point.

10.3 The appellant argued that D1 is the closest state of the art, from which the claimed subject-matter only differed by the amount of potassium ions, so that the problem was to provide a mere alternative dentifrice composition.

10.3.1 The dentifrice composition of D1 is only described as inhibiting the growth of dental plaque by maintaining a specific lamellar liquid crystal phase. There is no indication that Triclosan alone or a combination of Triclosan with potassium salt may have any desensitising effect. On that basis the technical problem to be solved over D1 may be seen in finding a dentifrice composition which has other use properties, namely desensibilizing properties. There is no hint in

D1 itself in which direction the dentifrice composition should be modified, to provide a desensibilizing property.

10.3.2 Although it is known from D2 that potassium citrate has a desensitising effect on sensitive teeth there is no incentive why the skilled person should combine this teaching with the specific Triclosan containing dentifrice compositions of D1, since D1 suggests several antimicrobial components other than Triclosan (see page 11, line 10 to page 12, line 35 and examples 3 and 4).

10.3.3 Therefore, even when starting from D1, as closest prior art, the claimed compositions is not made obvious.

10.4 From the above it follows that the subject-matter of claim 1 and the claims dependent thereon involves an inventive step.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

C. Eickhoff

R. Teschemacher