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Datasheet for the decision of 9 July 2024

Case Number: T 1050/22 - 3.3.07

Application Number: 16159225.8

Publication Number: 3045164

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Language of the proceedings: EN

Title of invention:
AQUEOUS PHARMACEUTICAL COMPOSITIONS CONTAINING BORATE-POLYOL COMPLEXES

Patent Proprietor:
NOVARTIS AG

Opponent:
Generics UK Ltd

Headword:
AQUEOUS PHARMACEUTICAL COMPOSITIONS CONTAINING BORATE-POLYOL COMPLEXES/Generics UK Ltd

Relevant legal provisions:
RPBA 2020 Art. 12(6)
EPC Art. 76(1), 56

Keyword:
Main request and auxiliary requests 1-12, 14-18, 20-23 - Amendments (No)
Admission of a new docuemnt (No)
Auxiliary requests 13 and 19 - Inventive step (No)

Decisions cited:
G 0002/10, T 1511/07, T 1731/18, T 1408/21, T 0249/19

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Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1050/22 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 9 July 2024

Appellant: (Opponent)	Generics UK Ltd Trident Place Mosquito Way Hatfield Hertfordshire AL10 9UL (GB)
Representative:	Gill Jennings & Every LLP The Broadgate Tower 20 Primrose Street London EC2A 2ES (GB)
Respondent: (Patent Proprietor)	NOVARTIS AG Lichtstrasse 35 4056 Basel (CH)
Representative:	Elkington and Fife LLP Prospect House 8 Pembroke Road Sevenoaks, Kent TN13 1XR (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 1 March 2022 rejecting the opposition filed against European patent No. 3045164 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	M. Steendijk
Members:	D. Boulois
	L. Basterreix

Summary of Facts and Submissions

I. European patent No. 3 045 164 based on the application 16 159 225.8 was granted on the basis of a set of 15 claims.

Independent claim 1 as granted read, with the addition of the marks (a)-(k) as also used by the opposition division (OD) in its decision:

"1. A multi-dose ophthalmic composition, comprising:
(a) brinzolamide, brimonidine or a combination thereof;
(b) an anionic polymer;
(c) a surfactant in a concentration of less than 0.1 w/v%;
(d) sodium chloride in a concentration of less than 0.4 w/v%;
(e) a first polyol, the first polyol being selected from mannitol, sorbitol or a combination thereof, wherein the concentration of the first polyol is at least 0.01 w/v% but less than 0.5 w/v%;
(f) a second polyol, the second polyol being selected from propylene glycol, glycerine or a combination thereof, wherein the concentration of the second polyol is at least 0.1 w/v% but less than 5 w/v % of the composition;
(g) an effective amount of borate, the effective amount being at least 0.05 w/v% but less than 0.5 w/v% of the overall composition;
(h) BAC as an anti-microbial preservative, the concentration of BAC in the composition being greater than 0.00001 w/v% but less than 0.0035 w/v%; and
(i) water,

(j) wherein a therapeutic agent is suspended in solution, and
(k) wherein the osmolality of the suspension is in the range of 240 to 360 mOsm."

II. The present patent was a divisional application of the application 14 150 085.1 having the publication and patent number EP 2 722 035 and of the application 10 727 317.9 having the publication number WO 2010/148190 and the patent number EP 2 442 790. The patent EP 2 722 035 is the subject of the decision T 249/19, which has been cited in this appeal proceedings.

III. The patent 3 045 164 B1 had been opposed under Article 100 (a) and (c) EPC on the grounds that its subject-matter lacked inventive step and extended beyond the content of the application as filed.

IV. The present appeal lies from the decision of the Opposition Division to reject the opposition (Article 101(2) EPC).

V. The documents cited during the opposition proceedings included the following:

D1: US 5 505 953
D2: Lester M., Clinical Ophthalmology 2008, 2(3), 517-523
D3: Remington, The Science and Practice of Pharmacy, 20th Ed., 2000, pages 829-830
D4: WO 2008/036847 A2
D5: WO 2010/148190 A1 (grandparent application)
D6: EP 2722035 A1 (parent application)
D7: Glaucoma Medical Therapy, Principles and Management, Ophthalmology Monographs, The Foundation of

the American Academy of Ophthalmology, Netland P.A. and Allen R.C. (eds), 1999, Section 1-3, page 9
D8: Pharmaceutical codex, 12th Ed., Lund W. (ed), 1994, pages 312-313
D9: Simbrinza (TM), prescribing information / product leaflet, April 2013.

VI. According to the decision under appeal, the subject-matter defined in claim 1 of the patent as granted was covered in an individualised manner by the combination of claims 1, 3, 7, 13, 14 ,15, and 18 of the earliest patent application as originally filed, with a pointer for the combination in Table H, and a basis for the concentration of borate of "at least 0.05 w/v%" on page 8, paragraph 3. Since the disclosure of the earliest application 10 727 317.9 was identical to the disclosure of the divisional application corresponding to the contested patent, the requirements of both Articles 76(1) and 123(2) EPC were met.

D1 was the closest prior art, in particular in view of formulations 9 and 10. The opposition division concurred with the formulation of the problem as given by the patent proprietor, namely the provision of a (further) safe (in terms of antimicrobial preservation and eye toxicity), comfortable (in terms of tolerability and resistance to tear PH normalization), and effective multi-dose ophthalmic formulation for the chronic treatment of glaucoma. The claimed solution was not obvious in view of in particular D1 and D4.

VII. The opponent (hereinafter the appellant) filed an appeal against said decision. With the statement setting out the grounds of appeal dated 8 July 2022, the appellant submitted the following items of evidence:

D10: Minutes of the oral proceedings in respect of T 249/19 issued on 11 March 2022
D11: Debbash et al. (2002), "Cytoprotective effects of Hyaluronic acid and Carbomer 934P in Ocular Surface Epithelial Cells", Investigative Ophthalmology and Visual Science (2002), 43:3409-3415.

VIII. In its reply to the statement of grounds of appeal dated 23 November 2022, the patent proprietor (hereinafter the respondent), submitted auxiliary requests 1-5 and requested that D11 not be admitted into the appeal proceedings.

The subject-matter of claim 1 of the auxiliary requests read as follows, the difference with respect to the main request being indicated in **bold:**

Auxiliary request 1

"...
(e) a first polyol, the first polyol being selected from mannitol, sorbitol or a combination thereof, wherein the concentration of the first polyol is at least 0.01 w/v% but less than **0.35 w/v%**;..."

Auxiliary request 2

"...
(b) **carboxyvinyl polymer in a concentration of at least 0.05 w/v% and less than 4.0 w/v**% ...
(e) a first polyol, the first polyol being selected from mannitol, sorbitol or a combination thereof, wherein the concentration of the first polyol is at least 0.01 w/v% but less than **0.35 w/v%**;..."

Auxiliary request 3

"...
(b) **carboxyvinyl polymer in a concentration of at least 0.2 w/v% and less than 0.7 w/v**% ...
(e) a first polyol, the first polyol being selected from mannitol, sorbitol or a combination thereof, wherein the concentration of the first polyol is at least 0.01 w/v% but less than **0.35 w/v%**;..."

Auxiliary request 4

"...
(b) **carboxyvinyl polymer in a concentration of at least 0.2 w/v% and less than 0.7 w/v**% ...
(e) a first polyol, the first polyol being selected from mannitol, sorbitol or a combination thereof, wherein the concentration of the first polyol is at least 0.01 w/v% but less than **0.35 w/v%**;...
(g) an effective amount of borate, the effective amount being at least **0.25 w/v%** but less than 0.5 w/v% of the overall composition;..."

Auxiliary request 5

"...
(a) **brinzolamide and brimonidine**;
(b) **carboxyvinyl polymer in a concentration of at least 0.2 w/v% and less than 0.7 w/v**% ...
(e) a first polyol, the first polyol being selected from mannitol, sorbitol or a combination thereof, wherein the concentration of the first polyol is at least 0.01 w/v% but less than **0.35 w/v%**;...
(g) an effective amount of borate, the effective amount being at least **0.25 w/v%** but less than 0.5 w/v% of the overall composition;..."

IX. With a letter dated 2 June 2023, the respondent made a request for correction under Rule 139 EPC with regard to the claimed unit mOsm, and submitted a new main request and new auxiliary requests 1-5 corresponding to the previous requests and comprising the following feature "wherein the osmolality of the suspension is in the range of 240 to 360 **mOsm/kg**" instead of "mOsm" in claim 1. The previously filed main request and auxiliary requests 1-5 were renumbered as auxiliary requests 6-11.

X. With a letter dated 12 September 2023, the appellant requested that the new requests not be admitted into the appeal proceedings and filed new documents:

D12: Practical Gastroenterology, July 2006, pages 46-68;
D13: Circulation Research, Volume XXIV, February 1969, pages 263-268;
D14: Pediatr. Rev., 2007, 28; 372-380.

XI. With a letter dated 18 December 2023, the appellant filed new documents:

D15: Koeppen and Stanton, 2013, Renal Physiology, 5th Ed., Philadelphia;
D16: Erstad, Pharmacotherapy, 2003.

XII. With a letter dated 21 December 2023, the appellant submitted decision T 249/19 relating to the parent patent having the patent number EP 2 722 035.

XIII. With a letter dated 1 February 2024, the respondent submitted new documents:

D17: CA 2088927
D18: WO 2004/073708
D19: Voight, 1987

XIV. A communication from the Board, dated 3 April 2024, was sent to the parties. In it, the Board expressed its preliminary opinion and questioned the compliance of the combination of features of claim 1 with Article 76(1) EPC, as well as the further combination with the features of dependent claim 11. Inventive step was assessed over D1 as closest prior art and the Board noted that D1, D2 and D4 appeared to render the claimed solution obvious.

XV. With a letter dated 20 May 2024, the respondent filed auxiliary requests 12 to 23.

Claim 1 of auxiliary requests 12-17 comprised all the following feature "wherein the osmolality of the suspension is in the range of 240 to 360 **mOsm/kg**" instead of "mOsm" , while claim 1 of auxiliary requests 18-23 kept the feature as granted "wherein the osmolality of the suspension is in the range of 240 to 360 **mOsm**".

The subject-matter of auxiliary requests 12-17 corresponded respectively to the subject-matter of the main request and auxiliary requests 1-5 with the deletion of dependent claim 11 or its corresponding dependent claim in each request, while the subject-matter of auxiliary requests 18-23 corresponded respectively to the subject-matter of auxiliary requests 6-11 with the deletion of dependent claim 11 or its corresponding dependent claim.

XVI. Oral proceedings took place on 9 July 2024.

XVII. The arguments of the appellant may be summarised as follows:

Admission of D11 into the appeal proceedings

The respondent knew this document since it had been filed for the parent case T 249/19. It could not be filed earlier, since the question of compatibility between BAC and carbomer was raised late in the other proceedings and was not raised in the summons of the OD (opposition division). Moreover, new auxiliary requests were filed in the present appeal proceedings, which justified the filing of this document.

Main request - Article 76(1) EPC

There was no basis for the combination of all features of claim 1. At least features (d), (e) and (g) were separately disclosed and it was not justifiable to combine them together and with the lower end of the concentration range of (h). There was no connection between the end points of the ranges. It was furthermore not possible to select lower and upper range limits of different compounds and to combine them together and there was no pointer for these combinations.

Auxiliary requests - Article 76(1) EPC

The arguments against the main request were equally valid against the auxiliary requests.

Auxiliary request 13 - Inventive step

The closest prior art was D1. The patent did not provide any comparative data and it was not possible to conclude that there was an improvement. Moreover, since the claimed subject-matter did not include the amounts of anionic polymer, it was not possible to conclude that adequate antimicrobial efficacy could be reached by the claimed composition. Compositions described in D1 had anyway the same level of antimicrobial efficacy. The claimed subject-matter was seen as an obvious aggregation of features, while each individual feature was known from the prior art, in particular D18, D19, D4, D3 or D8.

The same arguments applied for the other auxiliary requests, in particular auxiliary request 19.

XVIII. The arguments of the respondent may be summarised as follows:

Admission of D11 into the appeal proceedings

D11 could and should have been filed earlier, since it was known by the opponent as early as in 2019, when it was filed for the case T 249/19.

Main request - Article 76(1) EPC

Features (a), (b), (c), (f), (g), (h) except for the lower limit, (i), (j) and (k) found a basis in claims 1, 3, 7, 14, 15 and 18 of the earlier (grandparent) application D5. A basis for the features (d), (e), (h) and (l) could be found in the description of D5. Moreover, examples A, M and N could serve as pointers for the combination of features, while the claimed osmolality was inherent to the compositions. A basis

for claim 11 could also be found in the description of D5.

Auxiliary requests - Article 76(1) EPC

The arguments regarding the basis for the amendments of the main request were also valid for the auxiliary requests.

Auxiliary request 13 - Inventive step

The active agent defined for the claimed composition was not mentioned in document D1, which also did not mention any suspension. Moreover, the claimed composition differed from the compositions in document D1 in the nature and amounts of further defined ingredients, including the presence of an anionic polymer, the amount of the first polyol and the presence of a second polyol. The technical effects of the claimed subject-matter over D1 further included a reduction in toxicity and the compensation of the antimicrobial efficacy loss due to the lower concentration of BAC by the polyol/borate system which also provided a lower resistance to tear normalization. The effects were supported by the results in Table E and F of the patent. The problem was the provision of an ophthalmic composition that exhibits therapeutic efficacy in particular for the treatment of glaucoma, desired antimicrobial preservation properties, with low toxicity for direct and repeated eye application, having optimal viscosity and osmolality, which retains antimicrobial activity and buffer capacity and has low resistance to normalisation of tear pH and allowing the delivery of uniform content of active ingredients.

The same arguments applied for the other auxiliary requests, in particular auxiliary request 19.

XIX. Requests

The appellant requested that the decision under appeal be set aside and the patent be revoked. The appellant also requested that document D11 be admitted into the proceedings.

The respondent requested that the decision under appeal be set aside and the patent be maintained according to the set of claims filed as:
- main request or auxiliary requests 1-5 with letter of 2 June 2023
- auxiliary requests 6-11 corresponding to the main request (patent as granted) and auxiliary requests 1-5 filed on 23 November 2022
- auxiliary requests 12-23 filed on 20 May 2024.
The respondent also requested that document D11 not be admitted into the proceedings.

Reasons for the Decision

1. Admission of D11 into the appeal proceedings

1.1 D11 has been filed by the appellant with its statement of grounds of appeal dated 8 July 2022 and is a publication relating to experiments demonstrating the protective effect of hyaluronic acid and carbomer 934P against BAC toxicity in ocular epithelial cells.

The appellant considers this document as *prima facie* highly relevant with regard to the assessment of

inventive step, in the sense that it is likely to prejudice the maintenance of the patent. The filing of this document has in its view no adverse effect on procedural efficiency since its abstract provides a clear and concise synopsis of the experiments and its relevance will simplify the procedure.

1.2 In the present case, the opposition division sent its summons to oral proceedings on **13 August 2021**. In its annex to the summons, the opposition division considered that the opponent's allegations with regard to inventive step were without merit. The opposition division explained *inter alia* that the backbone of the problem-solution analysis starting from D1 as closest prior art and taking into account D4 is the same here as in the parent patent 14150805.1 (case T 249/19).

No oral proceedings took place during the opposition proceedings, since the opponent (appellant) announced in its letter dated 10 January 2022 that it would not be attending the scheduled oral proceedings of 8 February 2022.

The opponent (appellant) did not provide further arguments or documents during the opposition proceedings. The oral proceedings were cancelled by the opposition division, which issued its decision on the basis of the written submissions.

In the parallel case 14 150 085.1 before the Board of Appeal bearing case number T 249/19, which involved issues very similar to the present case, the same appellant-opponent filed the same document as document F10, renumbered D31, **with its statement of grounds of appeal dated 29 March 2019**, more than two years before

the appellant filed its notice of opposition in relation to the present patent.

It appears therefore that document D11 was known to the appellant as early as in March 2019, and could have been filed in the present case at this stage, namely during the opposition proceedings, but that the appellant decided to file it only later during the present appeal proceedings. Moreover, since the appellant considers this document as *prima facie* highly relevant with regard to the assessment of inventive step, the appellant should indeed have filed the document during the opposition proceedings of the present case.

The Board cannot identify any circumstance justifying the filing and admittance of D11 which could and should have been filed earlier. The Board has therefore decided not to admit it in the appeal proceedings under Article 12(6) RPBA.

2. Main request - Article 76(1) EPC

2.1 The description of the grandparent application WO 2010/148190 (D5) and of the parent application (D6) are essentially identical. The assessment regarding Article 76(1) EPC is therefore presented with reference to D5.

2.2 Under Articles 100(c), 76(1) and 123(2) EPC, amendments can only be made within the limits of what a skilled person would derive directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing, from the whole of the application as filed, following the "Gold standard" of G 2/10.

In the present case, the relevant question is whether the combination of features of claim 1 of the main request can be derived directly and unambiguously from D5. In the Board's view, this is not the case for the combination of the features (e) and (g) and even less the case for the further combination with the features of dependent claim 11, which relates to the viscosity of the suspension which should be "greater than 0.03 Pas (30 cps)". Claim 11 is dependent on claim 10 which defines the viscosity as "greater than 0.02 Pas (20 cps) but less than 0.5 Pas (500 cps)".

2.3 Feature (e) relates in particular to the amount of the first polyol, i.e "(e) a first polyol, ... wherein the concentration of the first polyol is **at least 0.01 w/v%** but **less than 0.5 w/v%;**", said range "**less than 0.5 w/v%**" excluding explicitly the value of "0.5 w/v%" (emphasize added by the Board).

Claim 3 of D5 claims a range of "**at least 0.01 w/v%** but **no greater than 0.5 w/v%**", the feature "no greater than 0.5 w/v%" including however the range limit of "0.5 w/v%", which is not the case of the claimed feature "less than 0.5 w/v%".

A basis for "**less than 0.5 w/v%**" can only be found in the description on page 7, 4th paragraph. The passage on page 7 discloses however only lists of possible distinct upper and lower range limits of the amount of polyol, from which numerous partially overlapping sub-ranges may be created. Said passage reads: "The first polyol is typically at least about 0.01 w/v %, more typically at least about 0.15 w/v % and even more typically at least about 0.25 w/v % of the ophthalmic composition. The first polyol is also typically less

than about 5 w/v %, more typically less than about 1.6 w/v % and even more typically less than about 0.5 w/v % of the ophthalmic composition."

Hence, when taking the disclosure of page 7 as the basis, the claimed range results from a combination of the lower limit "at least 0.01 w/v%" with the upper limit "less than 0.5 w/v%" and must be seen as a selection among several possibilities.

The conclusion is the same when starting from the lower range limit of claim 3 of D5, i.e. **"at least 0.01 w/v%"** and combining it with the upper range limit of **"less than 0.5 w/v%"** taken out of the list of upper limits of page 7. The newly created range is a selection among several ranges that may be created through such combination.

2.4 Feature (g) relates to the amount of borate and reads "(g) an effective amount of borate, the effective amount being **at least 0.05 w/v%** but **less than 0.5 w/v**% of the overall composition".

Claim 1 of D5 related to "an effective amount of borate, the effective amount being **less than about 0.5 w/v**% of the overall composition". There is no disclosure of a specific lower range limit in claim 1 or any other claim of D5.

The description on page 8 of D5 provides lists of possible distinct upper and lower range limits of the amount of borate and reads: "Typically, for the present invention, the borate is **at least about 0.05 w/v %**, more typically at least about 0.1 w/v % and still more typically at least about 0.25 w/v % of the ophthalmic composition. Furthermore, the borate can advantageously

be less than about 0.75 w/v %, more typically less than about 0.5 w/v % and still more typically less than about 0.4 w/v %, and even possibly less than about 0.35 w/v % of the ophthalmic composition.".

Hence, starting from the disclosure in D5 of lists of particular lower and upper limits which are found either in claim 1 of D5 or on page 8, numerous partially overlapping sub-ranges may be created and the claimed range of "**at least 0.05 w/v%** but **less than 0.5 w/v**%" represents again a selection from the list of ranges which may emerge from the original disclosure.

2.5 Claim 11 further specifies the viscosity of the suspension and defines it as "**greater than 0.03 Pas (30 cps)**". Claim 11 refers to dependent claim 10, which relates to a viscosity "greater than 0.02 Pas (20cps) but less than 0.5 Pas (500 cps)", creating for this reason a range of "greater than 0.03 Pas to less than 0.5 Pas".

The subject-matter of dependent claim 11 was not defined in the original claims of D5, but addressed in the description. The description of D5 gives on page 12 lists of lower and upper values of viscosity: "The viscosity of the suspension is typically greater than 5 cps, more typically greater than 20 cps and even more typically **greater than 30 cps**. The viscosity of the suspension is typically less than 1000 cps, more typically less than 500 cps and even more typically less than 150 cps".

The claimed feature of "greater than 0.03 Pas" is therefore a selection among several possible disclosed lower and upper values of viscosity ranges, picked out from the description and combined with an arbitrary

upper range limit as defined in claim 10. This feature constitutes again a selection from the list of possible ranges which may emerge from the original disclosure.

2.6 The selection of originally explicitly disclosed limit values defining several (sub)ranges to define an individual range may not necessarily generate subject-matter extending beyond the original disclosure, but the further combination of such individual range with another individual range emerging from a second list of ranges and relating to a different feature is not considered to be derivable from the original disclosure, unless there is a clear pointer to such a combination (see for instance T 1511/07 point 2.1,, T 1731/18, point 1.5 of the reasons, and the Case Law of the Boards of Appeal, 10th edition, 2022 II.E.1.6.2.a). In the present case, the basis for the definition of the indicated combination of ranges is even less evident due to the presentation in the claims and the description of D5 of lists of upper and lower limits rather than defined ranges (Cf. T 1408/21 point 1.4 and see the Case Law of the Boards of Appeal, 10th edition, 2022 II.E.1.6.2.c).

A relevant pointer is usually a specific indication or teaching in the original application directing the skilled person to a specific combination. Such specific indication can originate from the original claims and/or from disclosed specific embodiments, in particular when the examples of the application as filed present an uniform disclosure with regard to the concerned combination of features and all fall under the scope of the claims. However, the presence of discordant examples may well indicate that the examples do not provide any clear pointer to the combination of features.

In the present case, as explained above and starting from the disclosure in D5, feature (e) represents a first selection from the list of ranges which may emerge from the endpoints shown in claim 3 and page 7, while feature (g) represents a further selection from a second list of ranges that may be created on the basis of the endpoints shown in claim 1 and page 8 of D5. In the absence of any pointer to the particular combination of claim 1 of the main request, the combination of the range amounts for features (e) and (g) as claimed represents added subject-matter. The Board does indeed not identify any passage of the description or any example as possible pointer for the combination of such selections. Examples A, M and N, which were cited by the respondent, correspond to the only examples wherein the compounds and their amounts match with the claimed compounds and amounts. Most of the remaining examples, in particular examples B-K, show however discordant compositions, so that the examples cannot be seen as a clear pointer to the defined combination of features.

The combination of features (e) and (g) with the further selected feature of viscosity of dependent claim 11 is also considered not to be derivable from D5, since there is also no further pointer for such combination. Examples M and N cited by the respondent do even not indicate the viscosity of the compositions disclosed therein.

2.7 Consequently, the main request does not meet the requirements of Article 76(1) EPC.

Since the content of D5 is similar to the content of the divisional application as filed for which the

patent was granted, the same conclusion applies with regard to the requirements of Article 123(2) EPC.

3. Auxiliary requests 1 to 12 - Article 76(1) EPC

3.1 Auxiliary requests 1-3 still comprise the combination of feature (g) present in claim 1 with the viscosity feature present in respectively dependent claims 10 and 9 of auxiliary request 1 and auxiliary requests 2-3 corresponding to claim 11 of the main request. The subject-matter of these requests results therefore from multiple selections and does not meet the requirements of Article 76(1) EPC for the same reason as the main request.

3.2 Claim 1 of auxiliary request 4 has been amended *inter alia* by the amounts of borate which is now "(g)...at least **0.25 w/v%** but less than 0.5 w/v % of the overall composition". Said amendment originates from the description on page 8 and is still a combination of an upper and lower limit disclosed in this passage (cf. point 2.4 above) and remains a selection among several possibilities. Its combination with the subject-matter of dependent claim 9, corresponding to claim 11 as granted, represents still a combination of multiple selections, which is contrary to the requirements of Article 76(1) EPC.

3.3 In comparison to claim 1 of auxiliary request 4, claim 1 of auxiliary request 5 has furthermore been restricted to a combination of the active agents **"(a) brinzolamide and brimonidine"** which appears to be a selection among the possibilities given in claim 14 of D5, i.e. "brinzolamide, brimonidine or a combination thereof". The examples cannot serve as a pointer for this mixture of active agents, since only examples M

and N comprise it. The combination of the features (a), (b) and (g) in claim 1 and the subject-matter of dependent claim 9, corresponding to claim 11 as granted, represents a combination of multiple selections, which is contrary to the requirements of Article 76(1) EPC.

3.4 Auxiliary requests 6-11 correspond respectively to the main request and auxiliary requests 1-5 with the feature "mOsm" instead of its correction "mOsm/kg". The conclusions reached for the main request and auxiliary request 1-5 apply *mutatis mutandis* for auxiliary requests 6-11 which do therefore not meet the requirements of Article 76(1) EPC.

3.5 Claim 1 of auxiliary request 12 comprises the features "(e) a first polyol, the first polyol being selected from mannitol, sorbitol or a combination thereof, wherein the concentration of the first polyol is at least 0.01 w/v% but less than 0.5 w/v%" and "(g) an effective amount of borate, the effective amount being at least 0.05 w/v% but less than 0.5 w/v% of the overall composition" which constitute a combination of two selections. Auxiliary request 12 does therefore not meet the requirements of Article 76(1) EPC.

4. Auxiliary request 13 - Amendments

The subject-matter of claim 1 has been amended by the feature "(e) a first polyol, the first polyol being selected from mannitol, sorbitol or a combination thereof, wherein the concentration of the first polyol is at least 0.01 w/v% but **less than 0.35 w/v%;"**, which finds a direct basis in dependent claim 4 of D5, and is therefore not anymore a selection among numerous possible ranges from the description.

Claim 10 corresponding to claim 11 as granted has been deleted, so that the feature "(g) an effective amount of borate, the effective amount being at least 0.05 w/v% but less than 0.5 w/v% of the overall composition;" remains the unique selection made from D5. This single selection is directly and unambiguously derivable from the parent application, and since there is no combination with a second selection, the requirements of Article 76(1) EPC are met. The requirements of Article 123(2) EPC are met for the same reasons.

5. Auxiliary request 13 - Inventive step

5.1 The claimed invention relates to pharmaceutical compositions that contain borate-polyol complexes for improved preservation of the compositions. The patent seeks to develop means to enhance the antimicrobial activity of ophthalmic compositions comprising low concentrations of BAC while at the same time ensuring desirable buffering capacity of these compositions (see paragraphs [0009] and [0013] of the specification).

5.2 D1 is considered to represent the closest prior art, since it is related to the same technical purpose.

D1 discloses ophthalmic compositions comprising borate-polyol complexes which show increased antimicrobial activity as compared to boric acid or its salts: the borate-polyol complexes are formed by mixing boric acid and/or its salts with polyols such as mannitol, glycerine or propylene glycol in an aqueous solution (cf. col 1, last par. - col. 2, par. 3). The borate-polyol complexes are particularly useful in unpreserved saline solutions, but are also useful as adjunctive disinfecting agents in contact lens disinfecting

solutions containing *inter alia* benzalkonium chloride (BAC) (cf. col 2, lines 57-67). The borate-polyol complexes are utilized in an amount comprised between 0.5 to 6.0 wt% (cf. col 3, 2nd par.). D1 also recognizes that BAC has excellent antimicrobial activity but is toxic to sensitive tissues of the eye and can accumulate in contact lenses, and hence teaches to avoid use of toxic concentrations of BAC while not compromising antimicrobial efficacy (cf. col. 1 lines 44-57).

The compositions of D1 are useful as eyedrops, gels or ocular insert and will preferably also contain PVA or other viscosity enhancing polymers, such as cellulosic polymers or carboxyvinyl polymers (cf. col 3, lines 13-18).

Formulations 9 and 10 of D1 (cf. col 5-6) were mentioned by the opposition division in its decision:

	FORMULATION (percent by weight)								
INGREDIENT	1	2	3	4	5	6	7	8	9
PVA	0.75	1.4	0.75	0.75	0.75	0.75	0.75	0.75	0.75
Hydroxyethyl cellulose (HEC)	—	—	0.75	0.28	0.28	0.28	0.28	0.75	0.75
Mannitol	2.0	2.0	2.0	2.0	2.0	2.0	0.5	2.0	2.0
Boric acid	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35
Sodium borate	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
Edetate disodium	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Sodium chloride	0.09	0.09	0.09	0.09	0.45	0.09	0.09	0.09	0.09
Polyquad ®	0.001	0.001	0.001	0.001	0.001	0.001	0.001	—	—
Sucrose	—	—	—	—	—	2.5	—	2.5	2.5
Polyhexamethylene biguanide	—	—	—	—	—	—	—	0.0005	—
BAC	—	—	—	—	—	—	—	—	0.004

	FORMULATION (percent by weight)									
INGREDIENT	10	11	12	13	14	15	16	17	18	19
PVA	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4
Naphazolene HCl	0.1	0.1	—	—	—	—	—	—	—	—
Sodium sulfacetamide	—	—	—	10.0	—	—	—	—	—	—
Fluorometholone	—	—	—	—	0.1	—	—	—	—	—
Gentamycin sulfate	—	—	—	—	—	0.4	—	—	—	—
Levobunolol HCl	—	—	0.5	—	—	—	—	—	—	—
Mydrysone	—	—	—	—	—	—	1.0	—	—	—
Pilocarpine nitrate	—	—	—	—	—	—	—	1.0	1.0	1.0
Sodium metabisulfite	—	—	0.4	—	—	—	—	—	—	—
Mannitol	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	4.0	0.5
Boric acid	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.5
Sodium borate	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	—	—
Sodium chloride	0.45	0.45	0.45	—	0.45	0.45	0.45	0.45	—	—
Edetate disodium	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
BAC	0.004	—	—	—	—	—	—	—	—	—
Polyquad ®	—	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

5.3 The respondent has identified the following differences between the claimed subject-matter and the disclosure of D1:

- A multi-dose composition;
- (a) the presence of brinzolamide, brimonidine or a combination thereof as a therapeutic agent;
- (b) the presence of an anionic polymer;
- (c) the presence of a surfactant in a concentration less than 0.1 w/v%;
- (e) the concentration of the first polyol which is less than 0.35 w/v%;
- (g) the presence of a second polyol;
- (h) the concentration of BAC;
- (j) the active agent is suspended in solution;
- (k) the osmolality.

The Board agrees with the respondent with the exception of the feature relating to multi-dose composition. There is indeed no reason to doubt that the ophthalmic compositions disclosed in D1 can be utilized several times in particular in view of the presence of a

preservative system. The appellant identified also the same distinguishing features and the opposition division came to the same conclusion for the distinguishing features of claim 1 of the main request, which differed from claim 1 of auxiliary request 13 only in the higher amount limit of the first polyol.

5.4 During the opposition proceedings, the opposition division concurred with the respondent with regard to its definition of the problem for the subject-matter of claim 1 of the main request which had the same distinguishing features as claim 1 of the present request, namely the provision of a further safe (in terms of antimicrobial preservation and eye toxicity), comfortable (in terms of tolerability - resistance to tear pH normalization), and effective multi-dose ophthalmic formulation for the chronic treatment of glaucoma.

In the appeal proceedings, the respondent defined the problem as the provision of a safe, comfortable, and effective multi-dose ophthalmic formulation for the chronic treatment of glaucoma or the provision of an improved ophthalmic formulation for chronic treatment of glaucoma.

During the oral proceedings before the Board, the respondent defined furthermore the problem as the provision of an ophthalmic composition that exhibits therapeutic efficacy in particular for the treatment of glaucoma, desired antimicrobial preservation properties, with low toxicity for direct and repeated eye application, having optimal viscosity and osmolality, which retains antimicrobial activity and buffer capacity and has low resistance to normalisation

of tear pH and allowing the delivery of uniform content of active ingredients.

In the written proceedings, the appellant defined the problem as providing an alternative ophthalmic composition that avoids the use of toxic concentrations of BAC. During oral proceedings before the Board, the appellant agreed partially with the definition of the problem as defined by the respondent except on the points of the low toxicity and the uniform content of the amount of active delivered. The appellant did not agree that the compositions as claimed were improved ophthalmic compositions over the prior art.

5.5 The solution to any of these problems is a composition according to claim 1 comprising in particular brinzolamide, brimonidine or a combination thereof as a therapeutic agent suspended in solution, an anionic polymer, a surfactant in a specific concentration, a first polyol at a concentration of less than 0.35 w/v%, a second polyol, BAC at less than 0.0035 w/v%, at an osmolality as claimed.

5.6 Examples of the patent were cited by the respondent in support of a possible technical effect.

5.6.1 The respondent referred to two compositions falling within the scope of claim 1 of auxiliary request 13, namely compositions M and N in Table H.The patent shows in Table H that both compositions have a good antimicrobial efficacy over several microorganisms and that they exhibit a good resistance to tear PH normalization. There is however no comparison with other compositions in Table H, even less with compositions as disclosed in D1.

5.6.2 The respondent cited further Tables E and F of the patent as support of a technical effect.

In Table E, a composition E comprising the preservative components according to the invention is compared to compositions F and G. The addition of 0.75% w/v of a second polyol, i.e. propylene glycol, to a composition comprising 0.25% w/v of sorbitol in example E showed a clear improvement over compositions F and G, which respectively do not comprise any polyol or only 0.25% w/v of sorbitol. The experiments of Table E do however not show any comparison over compositions as disclosed in D1, i.e. comprising 2.00 w/v of only one polyol.

Table F provides a comparison between three compositions with regard to the antimicrobial efficacy. A composition I according to the invention and comprising 0.3 % w/v of boric acid, 0.3 % w/v of mannitol and 0.75% w/v of propylene glycol, was compared to a composition H comprising the same compounds but with 1.5% w/v of mannitol and a composition J with the same compounds but with 0.6% w/v of boric acid and 2.0 % w/v of mannitol. The results of Table F do not show a significant difference between the three compositions and tend to show that the concentration of the first polyol does not appear to have an effect on the antimicrobial efficacy as shown in Table F, since a composition with 2.0 wt% of mannitol has a similar antimicrobial efficiency as the two other compositions. In any case, the results cannot be exploited to show a comparison over compositions as disclosed in D1 with regard to the antimicrobial efficacy.

Accordingly, it is not possible to conclude on the basis of the examples of the patent that the claimed

ophthalmic composition provides an improvement over the closest prior art D1 with regard to properties of the composition, in particular the toxicity, antimicrobial efficacy and the resistance to tear PH normalization.

It is also not possible to conclude, as argued by the respondent, that the total effect of the combined differentiating features, i.e. the total effect of the composition, as compared to the prior art, provides an improvement compared to D1 in the absence of any evidence. It is in particular not possible to draw any conclusions with regard to any compensation of some loss of the antimicrobial efficacy of compositions comprising BAC due to the presence of an anionic polymer.

The only conclusion which can be drawn from the examples is that compositions according to the invention meet the requirements for preservation efficacy and provide a resistance to tear Ph normalization.

5.6.3 It remains to establish which technical effects may be credibly attributed to the identified distinguishing features.

(a) The presence of brinzolamide, brimonidine or a combination thereof **allows indeed a therapeutic efficacy in particular for the treatment of glaucoma.**

(b) The presence of an anionic polymer allows an increased viscosity, suspends the therapeutic agent for optimal therapeutic effect, and is compatible with the claimed BAC concentrations (see par. [0045] of the specification). While it is clear

that an anionic polymer such as carbomer allows the suspension of the active agent, there is no evidence of any further effect, especially **since the concentration of the anionic polymer is not claimed**. While it is known that anionic polymers may inactivate the antimicrobial efficacy of BAC (cf. D3, page 830), **there is no evidence that the presence of an anionic polymer decreases the antimicrobial efficacy of the whole preservative system comprising the borate/polyol system and BAC as described in document D1.**

(c) The presence of a surfactant at the claimed concentration assists the suspension of the active ingredients (see par. [0049]).

(d) The lower concentration of the first polyol credibly provides for a reduced resistance to normalization of tear pH. This effect appears to be confirmed by the teaching of D4 which was discussed during the oral proceedings before the Board, in particular Figure 3, which shows that **a composition comprising boric acid and 4% of sorbitol has a higher resistance to normalization of tear pH than similar compositions with only 0.25% or 1% of sorbitol.**

(e) The presence of a second polyol **enables credibly the reduction in concentration of the first polyol polymer to provide for reduced resistance to tear PH normalization of the borate/mono-polyol system.** There is however no evidence that the presence of a second polyol improves the antimicrobial efficacy over a system with 2.0 wt% of one unique polyol as disclosed in D1.

(f) With regard to the ocular toxicity linked with the lower concentration of BAC in the composition, the Board concurs with the conclusions of the opposition division in its decision in point 3.3.5 that **no particular effect or criticality has been shown to be associated with the cut-off limit of 0.0035 w/v % of BAC as compared to compositions of D1 comprising 0.004 wt.%.** A difference of 0.0005 w/v% in the concentration of BAC as compared to D1 is not shown to be linked to a decrease of toxic side effects, and cannot be regarded as allowing for a significant further reduction of BAC toxicity to sensitive eye tissues in patients receiving treatments for long periods of time. The Board notes furthermore that the concentration of BAC in D1 is already lower than the usual concentration of BAC in ophthalmic compositions which is commonly comprised between "0.005 to 0.02%" as disclosed in D3 on page 830. Moreover, D5 and the patent application disclosed that "BAC is generally used in the compositions of the present invention in an amount that is "less than about 0.005% w/v", which matched the BAC concentration in D1 (see page 6 of D5 or of the application as filed).

(g) **There does not appear to be any technical effect linked with the fact that the active ingredients are suspended.** There is no evidence that a suspension allows the delivery of a uniform content of active ingredients in comparison to a solution as in D1.

(h) The claimed osmolality allows **an increased patient comfort.**

5.6.4 In view of the technical effects provided by the distinguishing features, the Board concurs with the respondent with regard to the definition of the problem as it was given during oral proceedings, except for the delivery of uniform content of active ingredients, namely the provision of an ophthalmic composition that exhibits therapeutic efficacy in particular for the treatment of glaucoma, desired antimicrobial preservation properties, with low toxicity for direct and repeated eye application, having optimal viscosity and osmolality, which retains antimicrobial activity and buffer capacity and has low resistance to normalisation of tear pH.

5.7 With regard to obviousness, the relevant question is whether the skilled person would have contemplated a reduction of the amount of mannitol to less than 0.5 w/v%, by partially replacing mannitol with propylene glycol and/or glycerine, while at the same time further reducing the concentration of BAC to less than 0.0035 w/v%, in the presence of an anionic polymer and any of the defined suspended active agents, with a reasonable expectation of still meeting appropriate antimicrobial preservation.

In this context, several documents were discussed, namely D1, D2, D3, D4, D7, D8, D18, D19.

5.7.1 The main argument of the respondent is that any technical effect associated with individual distinguishing features over D1 could not be split up and that the nature and concentration of all the components have a combined effect.

According to the respondent, neither D1, nor any other cited prior art document provides any hints towards the

claimed combination of ingredients, let alone their concentrations, in particular for balancing the anti-microbial efficacy and potential toxicological effects of anti-microbial preservatives. In its view there was no hint that the low claimed concentrations for BAC and mannitol/sorbitol are sufficient for antimicrobial activity and avoid/minimise undesired effects, such as toxicity and resistance to normalisation of tear pH. In its view there was furthermore no hint that the claimed low concentrations of BAC are compatible with an anionic polymer viscosity enhancing agent which has an impact on the toxicity and loss of antimicrobial activity of BAC, that the low concentrations of surfactant avoid a negative effect on the preservation efficacy, and that low concentration of sodium chloride must be used in order to avoid an undesired decrease in viscosity.

5.7.2 The Board disagrees and considers that the subject-matter of claim 1 is a simple aggregation of known features and that the implementation of each feature is obvious in view of the cited prior art. There is in the Board's view no evidence of a general relationship between the effects from the distinguishing features.

The Board thus considers that, in the present case, the individual differentiating features are mostly responsible of specific individual technical effects, and not of a combined technical effect different from the sum of the technical effects of the individual features. These features and their related effects were *per se* known from either the closest prior art or from the additionally cited documents as it will be explained hereafter. The only related effects that can be acknowledged are the effects linked with the preservative system of borate/polyol and BAC; these

effects are however also obvious as it will be shown hereafter.

5.7.3 In the board's view, the claimed solution is obvious having regard to the cited state of the art. The reasons are as follows.

(a) D2 represents a review on the use of brinzolamide in ophthalmic suspensions, in particular for the treatment of open angle glaucoma and ocular hypertension. It mentions that brinzolamide is a white powder insoluble in water, commercially formulated as a 1% ophthalmic suspension to reduce intraocular pressure, with a pH of approximately 7.5 and osmolarity of 300 mOsm/kg (cf. page 517). It further adds that brimonidine can be used for the same treatment on page 521. In view of D2, **it was therefore known that at least brinzolamide is an active agent used in ophthalmic compositions in the treatment of glaucoma, exhibiting poor water solubility and has to be formulated in a suspension**. This common knowledge is reflected in the teaching of document D18 which discloses ophthalmic compositions comprising **brinzolamide alone or in combination with brimonidine suspended in a solution comprising a carbomer as viscosity agent and used *inter alia* in the treatment of glaucoma** (see examples 4-10 and the claims of D18). It was therefore also known from D18 to use anionic polymers such as carbomers as suspending agents for these active agents.

(b) Ophthalmic compositions comprising a borate-polyol complex for increasing the antimicrobial efficacy of other antimicrobial agents are known from D1 which mentions that said borate-polyol complexes

are even useful as such in unpreserved saline solutions, hence avoiding the use of further antimicrobial agents such as BAC (see col 2, lines 5-12 and 62-64). D1 discloses the same global amount of polyol and its ratio to borate in the composition as the defined amount of claim 1 of auxiliary request 13. Document D1 further describes the possible use of glycerine or propylene glycol as alternative polyols for mannitol (see D1, col. 2, l. 42-col. 3, l. 12). Even if polyvinyl alcohol (PVA) is the preferred viscosity enhancing agent in D1, the use of alternative viscosity enhancing agents such as carboxy vinyl polymers or cellulose derivatives is suggested in D1, such as in formulation 9 with the use of hydroxyethylcellulose (see col. 3, lines 13-17). The skilled person would not hesitate to add an anionic polymer in the form of a carboxy vinyl polymer to the compositions of D1, since the detrimental effects of anionic polymers on the antimicrobial activity of BAC appear to be linked with higher concentrations of BAC, i.e around 0.005-0.02 wt% as taught in D3 on page 830, and since the antimicrobial efficacy is ensured by the presence of the borate/polyol system. Moreover, many examples of D1 also comprise a surfactant in the presence of the viscosity-enhancing agent (cf. examples 4, 5, 8, 10, 12). **Consequently, the nature of the second polyol was known from D1, as was the use of carbomer and of a surfactant.**

(c) A borate-polyol system such as claimed is furthermore known from D4. The teaching of D4 is very close to the teaching of D1 and to the contested patent as it relates to self-preserved systems for ophthalmic compositions involving the

use of one or two polyols in combination with borate with very low concentrations of zinc ions (see page 1, 2nd par., page 2, 3d par. 6th par., page 9; page 5, lines 3-18). The teaching of D4 goes however beyond compositions comprising zinc anions, because D4 indicates the utility of a borate/polyol system to avoid large amounts of zinc, and other preservatives (see page 1, 2nd par. or page 2 last par.).

Moreover, Example Q on page 27 of D4 discloses specifically a composition comprising borate 0.25 wt.%, mannitol 0.1 wt.% and propylene glycol 1.6 wt.%, which corresponds qualitatively and quantitatively to the borate/polyol system of claim 1 of auxiliary request 13; the example, comprising also zinc chloride, shows further the anti-microbial effect of the composition. Examples T, U, V, W, Y of D4 show the same type of compositions. The compositions of D4 have an osmolality preferably comprised between 250 to 330 mOsm/kg.

Importantly, D4 teaches that **the lower amount of the first polyol, mannitol or sorbitol, in the composition allows for a low resistance to normalization to tear pH**, whereas the higher amount of the second polyol, propylene glycol, has minimal effect on resistance to normalization to tear pH. In particular, Figures 1 and 2 of document D4 show that a composition of 0.25 w/v% boric acid alone has practically no buffering capacity over a pH range of 6 to 7.5 while adding 0.25 w/v% of mannitol to this composition considerably enhances the buffering capacity of borate and hence the composition's resistance to normalisation of tear

pH. In view of this disclosure, the skilled person would have known that mannitol directly impacts the buffering capacity of borate and therefore the resistance to normalisation of tear pH after application of the composition to the patient's eye. The use of a system of a first and second polyol in association with boric acid is therefore known from D4 to be associated with the advantage of a reduced resistance to normalization to tear pH. **Hence, in view of Figures 1-3 and the explanations on pages 9-10 of D4, it was an obvious course of action to reduce the amount of mannitol in the formulations 9 and 10 of document D1 and to compensate it with a propylene glycol as second polyol.**

(d) As for the claimed concentration of BAC of lower than 0.0035 w/v%, this is merely an arbitrary modification of the 0.004 w/v% BAC used in formulations 9 or 10 of examples 2 and 3 of document D1, which a person skilled in the art would arrive at in a routine manner in view of the teaching of document D1 that borate-polyol compositions could even be used in the absence of further antimicrobial agent. As discussed above, D1 even envisages the use of the borate/polyol preservative system without any further classical preservative, and **there is no evidence that such composition would not meet the requirements of antimicrobial efficacy, which was not contested by the respondent.**

(e) D7 discloses that the tear osmolality corresponds to the claimed osmolality of the composition (see page 9). This information is confirmed by the osmolality of the compositions disclosed in D4. The

claimed osmolality is therefore considered as common for ophthalmic compositions.

5.7.4 In the light of the above considerations, it would have been straightforward for the skilled person faced with the objective technical problem to make the following modifications to formulations 9 or 10 of document D1, namely reducing the concentration of BAC in this formulation, replacing naphazoline HCl with brimonidine and/or brinzolamide in a suspension, selecting an anionic polymer and a surfactant as a suspension aid for brimonidine and/or brinzolamide instead of PVA, lowering the concentration of mannitol from 2.0 w/v% to less than 0.35 w/v% to reduce the formulation's resistance to normalisation of tear pH and adding propylene glycol in an amount falling within the range recited in claim 1 to ensure an adequate antimicrobial efficacy, and finally adapting the osmolality to the common values.

Consequently, the subject-matter of claim 1 of auxiliary request 13 does not involve an inventive step (Article 56 EPC).

The Board notes that the Board 3.3.01 came to the same conclusion in the parent case T 249/19.

6. Auxiliary requests 14-18 - Article 76(1) EPC

6.1 The subject-matter of auxiliary request 14 corresponds to the subject-matter of auxiliary request 2 with the deletion of dependent 9, corresponding to claim 11 of the main request, but still comprising the feature (g), i.e. "(g) an effective amount of borate, the effective amount being at least 0.05 w/v% but less than 0.5 w/v%

of the overall composition;" resulting from a selection.

Claim 1 of this request has been furthermore amended by the feature "(b) carboxyvinyl polymer in a concentration of at least 0.05 w/v% and less than 4.0 w/v%" originating from the description of D5 on page 12 which reads: "The amount of carboxyvinyl polymer present in the pharmaceutical composition of the present invention is typically at least about **0.05 %**, more typically at least about 0.1% even more typically at least about 0.2%. Moreover, the amount of carboxyvinyl polymer present in the pharmaceutical composition of the present invention is typically less than about **4.0%**, more typically less than about 1.2% even more typically less than about 0.7%." (emphasize added by the Board).

The claimed range of carboxyvinyl polymer results therefore from the combination of a lower limit and an upper limit from the disclosure of page 12 of D5. This combination of the more preferred lower limit with the most preferred upper limit does not *per se* introduce added subject-matter, but it must be seen as a selection out of the various ranges which may be created from the general, more preferred and most preferred ranges. No preference for this newly created range can be discerned in the parent application D5, since some examples do even not comprise a carboxyvinyl polymer (cf. examples D-G). Its combination with the other selected feature (g) results in the combination of multiple selections, which is contrary to the requirements of Article 76(1) EPC.

6.2 In auxiliary request 15, claim 1 has been amended in the amount of carboxyvinyl polymer, namely "(b)

carboxyvinyl polymer in a concentration of at least 0.2 w/v% and less than 0.7 w/v%" which constitutes a selection (cf. point 6.1 above). Its combination with the feature (g), i.e "(g) an effective amount of borate, the effective amount being at least 0.05 w/v% but less than 0.5 w/v% of the overall composition" in claim 1 results in the combination of multiple selections, which is contrary to the requirements of Article 76(1) EPC.

6.3 The same conclusion applies for auxiliary requests 16 and 17, which comprises the features "(b) carboxyvinyl polymer in a concentration of at least 0.2 w/v% and less than 0.7 w/v%" and "(g)...at least **0.25 w/v%** but less than 0.5 w/v % of the overall composition" in claim 1. The amendment regarding the amount of borate originates from the description on page 8 and is still a combination of an upper and lower limit disclosed in this passage (cf. point 2.4 above) and remains a selection among several possibilities. The combination of these two features represents still a combination of multiple selections, which is contrary to the requirements of Article 76(1) EPC.

6.4 Auxiliary request 18 corresponds to the main request with the feature "mOsm" instead of its correction "mOsm/kg" and with the deletion of dependent claim 11. Claim 1 comprises the features "(e) a first polyol, the first polyol being selected from mannitol, sorbitol or a combination thereof, wherein the concentration of the first polyol is at least 0.01 w/v% but less than 0.5 w/v%;" and "(g) an effective amount of borate, the effective amount being at least 0.05 w/v% but less than 0.5 w/v% of the overall composition;" which constitute a combination of multiple selections, which is contrary to the requirements of Article 76(1) EPC.

7. Auxiliary request 19

Claim 1 of auxiliary request 19 is identical to claim 1 of auxiliary request 13, with the exception of the absence of correction of the unit "mOsm/kg" present in auxiliary request 13, which remained "mOsm" in claim 1 of auxiliary request 19. Hence, the considerations set out above regarding the inventive step of claim 1 of auxiliary request 13 equally apply to claim 1 of auxiliary request 19, which therefore does not meet the requirements of Article 56 EPC.

8. Auxiliary requests 20-23 -Article 76(1) EPC

The subject-matter of auxiliary requests 20-23 corresponds respectively to the subject-matter of auxiliary requests 14-17 except for the absence of the correction of the unit "mOsm/kg". The conclusions reached for auxiliary requests 14-17 equally apply for auxiliary requests 20-23, which therefore do not meet the requirements of Article 76(1) EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

A. Vottner M. Steendijk

Decision electronically authenticated