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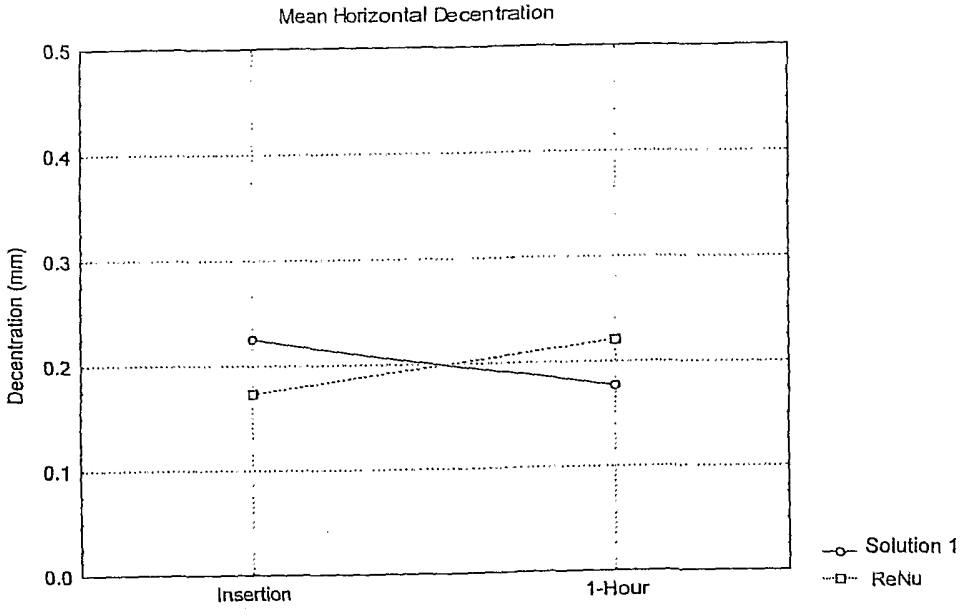
(54) Title: LENS CARE SOLUTIONS FOR HYDROGEL CONTACT LENSES



(57) Abstract: Contact lens cleaning and disinfecting compositions that reduce or eliminate wearer discomfort comprising a disinfecting amount of Alexidine. The solutions are effective in removing protein and lipid tear film deposits on both hard and soft contact lenses.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

LENS CARE SOLUTIONS FOR HYDROGEL CONTACT LENSES

Field of the Invention:

The present invention relates to the development of a gentle multi-purpose solution for hydrogel contact lenses. More particularly, the present invention relates to a multi-purpose solution for hydrogel contact lenses that is a gentle, "one bottle" system with "no-rub" disinfecting and passive cleaning for both lipid and protein depositions.

Background of the Invention:

When contact lenses are removed from the eyes, they often retain on their surface a deposit or proteinaceous, oily and sebaceous matter that, if not removed, greatly reduces wettability properties and optical clarity of the lenses. In the case of hard contact lenses fabricated from poly(methyl methacrylate), the lenses are of such firmness that they can be treated using mechanical devices to remove deposits of contamination from their surfaces. Likewise, because hard contact lenses do not absorb appreciable amounts of water, the selection of cleaning agents is relatively non-critical. In many instances, use of even harsh disinfecting and cleaning agents on hard contact lenses does not create a problem.

However, because of the hydrophilic properties of soft contact lenses formulated from materials such as poly(2-hydroxyethyl methacrylate), soft contact lenses do absorb more water than hard contact lenses. Consequently, greater care must be exercised in formulating cleansing solutions for soft contact lenses. With soft contact lenses, materials in the solutions can be absorbed and concentrated in the lenses which in-turn can damage the lens and even injure the eyes of the user.

In many instances, solutions intended for hard contact lenses are generally not adaptable for use with soft contact lenses. This may be illustrated, for instance, in the case of hard contact lens solutions containing benzalkonium chloride or chlorobutanol. If these hard contact lens solutions are used on soft contact lenses the solutions' important hydrophilic properties may be lost. Thus, in formulating contact lens care solutions, such as cleaning compositions, a number of factors need to be carefully weighed to assure total compatibility of the system in terms of functional efficaciousness, potential for damage to the lens and possible hazards to the wearer's eyes.

Multi-purpose solutions that clean and disinfect contact lenses have been described in the literature. For example, U.S. Patent Numbers 4,820,352 to Riedhammer et al. and 5,096,607 to Mowrey-McKee et al. disclose such solutions. More generally, contact lens solutions are disclosed in U.S. Patent Numbers 5,356,555 to Huth et al., 5,401,431 to Nakagawa et al., 5,409,546 to Nakagawa et al., 5,449,442 to Yamada et al., 5,487,788 to

Kamiya et al., 5,505,953 to Chowhan, 5,556,480 to Rontome et al., 5,607,908 to Potini et al., 5,630,884 to Huth, 5,648,074 to Park et al., 5,654,262 to Desai et al., 5,800,807 to Huth et al., 5,820,696 to Kimura et al., 5,858,937 to Richard et al., 5,922,279 to Spooner, 6,024,954 to Park et al., and 6,121,327 to Tsuzuki et al.

Many multi-purpose contact lens solutions require the user to apply the solution to the contact lens and then to rub the contact lens, either between two fingertips or between a fingertip and the palm of the other hand. This step is known as "digital rubbing", and enhances cleaning. Where a multi-purpose solution is effective to clean and disinfect contact lenses without rubbing, maintaining contact lenses is simpler and easier. Thus, it is desirable to provide a safe and effective solution for cleaning contact lenses that does not require digital rubbing.

Disinfecting agents can cause wearer discomfort. Thus, it would be desirable to provide a safe and effective solution for cleaning soft contact lenses that reduces wearer discomfort while still maintaining efficacy as a disinfectant.

Summary of the Invention:

This invention provides a multi-purpose solution that requires no digital rubbing, i.e., "no-rub", for disinfecting and cleaning both lipid and protein deposits from a contact lens, and reduces or eliminates wearer discomfort. Solutions of the present invention may likewise be useful as in-

eye conditioning solutions, in-eye cleaning solutions or in-eye cleaning and conditioning solutions for contact lens wearers. Solutions of the present invention may also be useful as in-eye drops, which condition the contact lens, and may also clean the contact lens. Such in-eye drops include antimicrobial agents for preservation of the solution, not for disinfection of a contact lens while being worn in an eye.

Loss of tight junctions and defects in the integrity of the corneal epithelium can be detected in some cases using a sodium fluorescein solution and visualizing the staining of the stroma by a slitlamp fluorometer. The composition of the present invention preferably comprises about 4.0 to about 5.0 ppm Alexidine. Alexidine has been associated with reduced or eliminated levels, of even non-clinically significant trace levels, of corneal and/or conjunctival staining, which is unexpected since other biguanides may cause such staining. The compositions of the present invention also exhibited greater comfort when compared with other no-rub multi-purpose solutions such as Opti-Free™ (Alcon Laboratories, Inc., Fort Worth, Texas), which contains Polyquaternium-1 as a disinfecting agent.

Brief Description of the Drawings:

FIGURE 1 is a graph of mean horizontal decentration vs. decentration for test and control solutions at insertion and 1-hour;

FIGURE 2 is a graph of mean movement vs. movement for test and control solutions at insertion and 1-hour;

FIGURE 3 is a graph of mean inferior overlap vs. overlap for test and control solutions at insertion and 1-hour;

FIGURE 4 is a graph of mean comfort vs. analog comfort for test and control solutions at insertion and 1-hour;

FIGURE 5 is a graph of mean pre-lens tear film break-up time (TBUT) vs. break-up time (BUT) for test and control solutions at insertion and 1-hour;

FIGURE 6 is a graph of mean horizontal decentration vs. decentration for test and control solutions at insertion and 1-hour;

FIGURE 7 is a graph of mean movement vs. movement for test and control solutions at insertion and 1-hour;

FIGURE 8 is a graph of mean inferior overlap vs. overlap for test and control solutions at insertion and 1-hour;

FIGURE 9 is a graph of mean comfort vs. analog comfort for test and control solutions at insertion and 1-hour; and

FIGURE 10 is a graph of mean pre-lens tear film break-up time (TBUT) vs. break-up time (BUT) for test and control solutions at insertion and 1-hour.

Detailed Description of the Invention:

The present invention provides no-rub multi-purpose contact lens solutions for disinfecting and cleaning both lipid and protein deposits from a contact lens. The subject solutions provide greater lens comfort to the contact lens wearer.

Compositions employed in this invention are aqueous solutions. Compositions of the present invention are preferably used as multi-purpose contact lens solutions to clean and disinfect soft-type contact lenses manufactured from hydrogel biomaterials such as for example but not limited to silicone hydrogel biomaterials. Silicone hydrogel contact lenses include for example but are not limited to contact lenses manufactured from siloxy-containing monomers, siloxy-containing macromolecular monomers, and copolymers with fluoro-containing monomers, alkyl-, cycloalkyl-, arylalkyl- and aryl-containing derivatives of acrylic or methacrylic acid, or itaconic acid, as well as styrenes, butudienes or isoprenes. Such systems could also be copolymerized with hydrophilic monomers such as 2-hydroxyethyl methacrylate, N-vinylpyrrolidone, N,N-dimethylacrylamide and (meth)acrylic acid.

Compositions of the present invention preferably include one or more polyethers. Polyethers employed in the subject compositions may include for example but are not limited to polyethers based upon poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide), i.e., (PEO-PPO-PEO), or poly(propylene oxide)-poly(ethylene oxide)-poly(propylene oxide), i.e., (PPO-PEO-PPO), or a combination thereof. PEO-PPO-PEO and PPO-PEO-PPO, such as for example poloxamers and poloxamines, are commercially available under the trade names Pluronics™, R-Pluronics™, Tetronics™ and R-Tetronics™ (BASF Wyandotte Corp., Wyandotte, Michigan). Polyethers in the subject ophthalmic solutions exhibit ready absorption into hydrogel

biomaterials such as those used in the manufacture of soft-type contact lenses. Polyethers in the subject ophthalmic solutions, after absorption into hydrogel biomaterials to a high concentration, exhibit slow release from the hydrogel biomaterials over a period of time in an aqueous environment. In accordance with the present invention, the one or more polyethers release slowly from a worn contact lens into an eye's tear film over a long time period to produce longer lasting wetting performance, improved lubricity, improved end-of-the-day comfort and reduced feeling of dryness from wearing contact lenses.

Compositions of the present invention provide efficient performance at polyether surfactant concentrations ranging from as little as about 0.01 to about 15 weight percent by volume (w/v). Greater concentrations may be used, but provide no added benefit and only increase the potential for irritating eye tissues. More preferably, the solutions of the subject invention will contain from about 0.1 to about 5 weight percent polyether surfactant.

The subject compositions in addition to polyethers likewise include one or more, but at least one, cationic polyelectrolyte that functions to control lens swelling caused by the absorption of high concentrations of polyethers as disclosed in U.S. Patent Application Serial Number 10/392,743, incorporated herein in its entirety by reference. By controlling lens swelling, visual acuity is maintained. Suitable cationic polyelectrolytes include for example but are not limited to polyquaternium 1, polyquaternium 10, polyquaternium 11, polyquaternium 16, polyquaternium 44 and

polyquaternium 46, but preferably polyquaternium 10 available under the trade name Polymer JR (BASF Wyandotte Corp.). Preferably, the ophthalmic solution of the present invention comprises about 0.001 to about 5 weight percent by volume and more preferably from about 0.01 to about 0.5 weight percent of one or more cationic polyelectrolytes for control of lens swelling.

To provide for both cleaning and disinfection of a contact lens in a single step, compositions of the present invention contain an antimicrobial agent. The use of Alexidine in formulations of the present invention is associated with reduced levels of corneal and/or conjunctival staining. It is unexpected that Alexidine would be associated with reduced or eliminated levels of corneal and/or conjunctival staining since other biguanides may cause such staining. Accordingly, Alexidine, its salts, non-polymeric, non-chloro-containing bis(biguanide)s, or combinations thereof, are the preferred antimicrobial agents, with Alexidine-2HCl being the most preferred. Preferably, the antimicrobial agent will be used in a disinfecting amount or an amount from about 0.0001 to about 0.5 weight percent by volume.

A disinfecting amount of an antimicrobial agent is an amount that will at least partially reduce the microorganism population in the formulations employed. Preferably, a disinfecting amount is that which will reduce the microbial burden by two log orders in four hours and more preferably by one log order in one hour. Most preferably, a disinfecting amount is an amount which will eliminate the microbial burden on a contact lens when used in the

regimen for the recommended soaking time as established by ISO (International Standards for Ophthalmic Optics)/FDA Stand-Alone Procedures for Disinfection Test (ISO/DIS 14729; 2001). Typically, such agents are present in concentrations ranging from about 0.00001 to about 0.5 weight percent based on volume (w/v), and more preferably, from about 0.00003 to about 0.05% weight percent.

Compositions of the present invention also include one or more but at least one osmolality agent in a concentration sufficient to increase the cleaning efficacy of the solution without adversely affecting the antimicrobial efficacy of the solution. Suitable osmolality agents include for example but are not limited to metal halides such as magnesium, calcium, sodium and potassium chloride, diols and polyols such as propylene glycol and glycerin, mono-, di-, or polysaccharides (saccharides), such as dextrose and trehalose, as well as amino acids such as lysine. Such osmolality agents may be used individually or in combinations in amounts ranging from about 0.01 to about 2.5 weight percent by volume (w/v) and preferably so that the final osmotic value of the solution has an osmolality of more than 200 mOsm/kg, and preferably from 220 to 400 mOsm/kg, and more preferably from 220 to 320 mOsm/kg.

In order to maintain the pH of the solutions within the range of about 6.5 to 7.8, one or more suitable buffers may be added to the subject compositions. Examples of useful buffering agents include for example, but

are not limited to alkali metal salts such as potassium or sodium carbonates, acetates, borates, phosphates, and citrates, and weak acids such as acetic and boric acids. Preferred buffering agents include boric acid, sodium borate, potassium citrate, citric acid, sodium bicarbonate, including combinations of Na_2PO_4, NaH_2PO_4 and KH_2PO_4, and aminoalcohols. Generally, buffers will be used in amounts ranging from about 0.01 to about 2.5, and preferably, from about 0.1 to about 1.5 percent by weight/volume (w/v).

Compositions of the present invention are described in still greater detail in the examples provided below. However, it is to be understood that the following examples are for illustrative purposes only and do not purport to be wholly definitive as to conditions and scope of the present invention.

EXAMPLE 1 – Clinical Performance Study:

A test solution, i.e., Solution 1, was prepared as set forth below in Table 1 and compared against that of ReNu™ MultiPlus No Rub Formula Multi-Purpose Solution (Bausch & Lomb, Incorporated), hereinafter, "ReNu MultiPlus", in a clinical performance study.

TABLE 1

Test Solutions

Ingredients	ReNu MultiPlus (% W/W)	Solution 1 (% W/W)
Pluronic F127	0	2.00
Tetronic 1107	1.00	1.00
Sodium Chloride	0.49	0.09
Boric Acid	0.64	0.85
Sodium Borate	0.09	0
EDTA	0.11	0
Sodium Phosphate (monobasic)	0	0.15
Sodium Phosphate (dibasic)	0	0.31
Polymer JR	0	0.02
PHMB HCl	1.1 ppm	0
Alexidine 2HCl	0	4.5 ppm
Dequest 2016	0.10	0.10
Purified Water	Q.S. to 100 gm	Q.S. to 100 gm

EDTA = Ethylenediaminetetraacetic acid
PHMB HCl = poly(hexamethylene biguanide)
Dequest™ 2016 (Solutia Inc., St. Louis, Missouri)

The objective of this study was to assess the short-term (1-hour) clinical performance of Solution 1 as compared to ReNu MultiPlus when used with PureVision™ lenses (Bausch & Lomb, Incorporated). To this end, twenty-four (24) subjects, all habitual soft spherical contact lens wearers, were enrolled in the study. The test solution, Solution 1, was prepared in accordance with the present invention. The control solution, ReNu MultiPlus, was taken from inventory (lot # GL2029). The lenses used in this study were standard PureVision lenses taken from inventory.

Each well of each of the Bausch & Lomb lens cases was pre-treated using a single, 4-hour minimum soak, with either Solution 1 or ReNu MultiPlus. For each case, the well treated with Solution 1 was randomly determined and the fellow well received ReNu MultiPlus. All PureVision lenses were pre-treated using two separate, 4-hour minimum soaks, with either Solution 1 or ReNu MultiPlus, in the pre-treated lens cases, following the same randomization used for the lens case wells.

Each subject was fitted with a pre-treated lens pair. Each lens was evaluated for centration, movement, comfort, wetting, deposits and pre-lens tear film break-up time. Each subject wore a Solution 1/PureVision lens and a ReNu MultiPlus/PureVision lens on contralateral eyes for approximately 1 hour. The eyes receiving Solution 1/PureVision lenses were randomly assigned. Subjects and the investigator were masked to solution identity. Testing was repeated after 1 hour of lens wear.

Unless otherwise noted, a 2-way repeated measures ANOVA incorporating the factors Time (insertion and 1-hour) and Solution (Solution 1 – test vs. ReNu MultiPlus – control) was used to test for differences in means for each of the parametric dependent variables. The data for each of the ordinal dependent measures, i.e., those assigned a clinical grade, were analyzed using the Wilcoxon Matched Pairs procedure. Differences at the alpha = 0.05 level were considered to be statistically significant.

There was a statistically significant difference in mean horizontal decentration with respect to the Time x Solution effect (ANOVA, $p<0.005$): lenses pre-treated with test solution had a slight decrease in decentration while those pre-treated with control solution had a slight increase in decentration. There were no significant differences noted with respect to the Time and Solution effects (ANOVA, $p>0.89$ in both cases) as illustrated in Figure 1.

There was a statistically significant difference in mean movement with respect to the Time effect (ANOVA, $p<0.003$): all lenses, both those pre-treated with test and pre-treated with control solutions, exhibited less movement at 1-hour than at insertion. There were no significant differences noted with respect to the Solution and Time x Solution effects (ANOVA, $p>0.77$ in both cases) as illustrated in Figure 2.

There was a statistically significant difference in mean inferior overlap with respect to the Time and Solution effects (ANOVA, $p<0.004$ in both cases): all lenses, both those pre-treated with test and pre-treated with

control solutions, exhibited less inferior overlap at 1-hour than at insertion. The lenses pre-treated with Solution 1 exhibited less inferior overlap when compared to lenses pre-treated with ReNu MultiPlus. There was no significant difference noted with respect to the Time x Solution effect (ANOVA, $p>0.75$) as illustrated in Figure 3.

There was no statistically significant difference in mean comfort with respect to the Time, Solution, and Time x Solution effects (ANOVA, $p>0.09$ in all cases) as illustrated in Figure 4.

There was a statistically significant difference in mean break-up time with respect to the Time effect (ANOVA, $p<0.01$): all lenses, both those pre-treated with Solution 1 and pre-treated with ReNu MultiPlus, exhibited less break-up time at 1-hour than at insertion. There were no significant differences noted with respect to the Solution and Time x Solution effects (ANOVA, $p>0.10$ in both cases) as illustrated in Figure 5.

There was no statistically significant difference between the test and control solutions for lens surface wettability (Wilcoxon Matched Pairs, $p>0.90$ in all cases).

There was no statistically significant difference between the test and control solutions for lens surface deposition (Wilcoxon Matched Pairs, $p>0.18$ in all cases).

In summary, twenty-four subjects were enrolled in a 1-hour, non-dispensing evaluation comparing Solution 1 (test solution) to ReNu MultiPlus (control solution) using PureVision lenses. The test solution exhibited

statistically significant less lens inferior overlap when compared to the control solution. There were no statistically significant differences noted between the solutions with respect to lens horizontal decentration, lens movement, comfort, pre-lens tear film break-up time, lens wettability and lens deposition. All study results are set forth below in Table 2.

TABLE 2

Study of Solution 1 Compared to ReNu MultiPlus Using PureVision Lenses

Summary of Results

Insertion	Valid N	Mean	Minimum	Maximum	Std. Dev.
Movement TI	24	0.51	0.20	1.40	0.30
Movement CI	24	0.51	0.20	1.40	0.26
Inferior overlap TI	24	1.75	1.20	2.60	0.33
Inferior overlap CI	24	1.85	1.20	2.60	0.34
Decentration TI	24	0.23	0.00	0.60	0.15
Decentration CI	24	0.17	0.00	0.50	0.12
Analog comfort TI	24	93.96	76.00	99.00	6.08
Analog comfort CI	24	93.08	75.00	99.00	6.78
TBUT TI	24	11.50	6.00	28.00	5.36
TBUT CI	24	13.50	6.00	29.00	6.38
Wettability TI	24	0.00	0.00	0.00	0.00
Wettability CI	24	0.00	0.00	0.00	0.00
Deposition TI	24	0.04	0.00	1.00	0.20
Deposition CI	24	0.08	0.00	1.00	0.28

TABLE 2 - Continued

Insertion Dev.	Valid N	Mean	Minimum	Maximum	Std.
1-Hour					
Movement TI	24	0.41	0.10	1.40	0.30
Movement CI	24	0.39	0.10	0.80	0.20
Inferior overlap TI	24	1.67	1.00	2.20	0.33
Inferior overlap CI	24	1.75	1.20	2.40	0.35
Decentration TI	24	0.18	0.00	0.40	0.12
Decentration CI	24	0.22	0.00	0.60	0.16
Analog comfort TI	24	94.96	80.00	99.00	6.06
Analog comfort CI	24	94.83	81.00	99.00	6.08
TBUT TI	24	10.17	5.00	19.00	3.45
TBUT CI	24	10.29	6.00	23.00	4.63
Wettability TI	24	0.13	0.00	1.00	0.34
Wettability CI	24	0.13	0.00	1.00	0.34
Deposition TI	24	0.04	0.00	1.00	0.20
Deposition CI	24	0.21	0.00	2.00	0.51

TI = Test Solution 1/PureVision lenses
CI = Control ReNu MultiPlus/PureVision lenses

EXAMPLE 2 – Clinical Performance Study:

A test solution, i.e., Solution 1, was prepared as set forth above in Table 1 and compared against that of Opti-Free Express™ No Rub Multi-Purpose Disinfecting Solution (Alcon Laboratories, Incorporated), hereinafter, "Opti-Free", in a clinical performance study.

The objective of this study was to assess the short-term (1-hour) clinical performance of Solution 1 as compared to Opti-Free when used with PureVision™ lenses (Bausch & Lomb, Incorporated). To this end, twenty-four (24) subjects, all habitual soft spherical contact lens wearers, were enrolled in the study. The test solution, Solution 1, was prepared in accordance with the present invention. The control solution, Opti-Free, was taken from inventory (lot # 33813F). The lenses used in this study were standard PureVision lenses taken from inventory.

Each well of the Bausch & Lomb lens cases was pre-treated using a single, 4-hour minimum soak, with either Solution 1 or Opti-Free. For each case, the well treated with Solution 1 was randomly determined and the fellow well received Opti-Free. All PureVision lenses were pre-treated using two separate, 4-hour minimum soaks, with either Solution 1 or Opti-Free, in the pre-treated lens cases, following the same randomization used for the lens case wells.

Each subject was fitted with a pre-treated lens pair. Each lens was evaluated for centration, movement, comfort, wetting, deposits and pre-lens tear film break-up time. Each subject wore a Solution 1/PureVision lens and

a Opti-Free /PureVision lens on contralateral eyes for approximately 1 hour. The eyes receiving Solution 1/PureVision lenses were randomly assigned. Subjects and the investigator were masked to solution identity. Testing was repeated after 1 hour of lens wear.

Unless otherwise noted, a 2-way repeated measures ANOVA incorporating the factors Time (insertion and 1-hour) and Solution (Solution 1 – test vs. Opti-Free – control) was used to test for differences in means for each of the parametric dependent variables. The data for each of the ordinal dependent measures, i.e., those assigned a clinical grade, were analyzed using the Wilcoxon Matched Pairs procedure. Differences at the alpha = 0.05 level were considered to be statistically significant.

There was a statistically significant difference in mean horizontal decentration with respect to the Time effect (ANOVA, $p<0.03$): all lenses, both those pre-treated with test and pre-treated with control solutions, exhibited greater decentration at 1-hour than at insertion as illustrated in Figure 6. No significant differences were noted between test and control solutions.

There was a statistically significant difference in mean movement with respect to the Time and Solution effects (ANOVA, $p<0.008$ in both cases). All lenses, both those pre-treated with test solution and pre-treated with control solution, exhibited less movement at 1-hour than at insertion. The lenses pre-treated with test solution exhibited less movement when compared to lenses pre-treated with control solution as illustrated in Figure

7. Mean lens movement was 0.40 mm and 0.48 mm for test and control solutions, respectively.

There was a marginally statistically significant difference in mean inferior overlap with respect to the Time effect (ANOVA, $p<0.06$): all lenses, both those pre-treated with test and pre-treated with control solutions, exhibited less inferior overlap at 1-hour than at insertion. No significant differences were noted between test and control solutions as illustrated in Figure 8.

There was a statistically significant difference in mean comfort with respect to the Solution effect (ANOVA, $p<0.05$). The test solution exhibited greater comfort when compared to the control solution. Mean comfort was 94.94 and 93.06 for test and control solutions, respectively, as illustrated in Figure 9.

There was no statistically significant difference in mean break-up time with respect to the Time, Solution, and Time x Solution effects (ANOVA, $p>0.09$ in all cases) as illustrated in Figure 10.

There was no statistically significant difference between the test and control solutions for lens surface wettability (Wilcoxon Matched Pairs, $p>0.11$ in all cases).

There was no statistically significant difference between the test and control solutions for lens surface deposition (Wilcoxon Matched Pairs, $p>0.59$ in all cases).

In summary, twenty-four subjects were enrolled in a 1-hour, non-dispensing evaluation comparing Solution 1 (test solution) to Opti-Free

(control solution) using PureVision lenses. The test solution exhibited statistically significant less lens movement and greater comfort when compared to the control solution. There were no statistically significant differences noted between the test and control solutions with respect to lens centration, pre-lens tear film break-up time, lens wettability and lens deposition. All study results are set forth below in Table 3.

TABLE 3

Study of Solution 1 Compared to Opti-Free Using PureVision Lenses

Summary of Results

Insertion	Valid N	Mean	Minimum	Maximum	Std. Dev.
Movement TI	24	0.47	0.20	1.20	0.26
Movement CI	24	0.54	0.20	1.20	0.24
Inferior overlap TI	24	1.75	0.80	2.60	0.40
Inferior overlap CI	24	1.82	1.00	2.80	0.42
Decentration TI	24	0.14	0.00	0.30	0.09
Decentration CI	24	0.20	0.00	0.45	0.13
Analog comfort TI	24	95.42	68.00	99.00	7.88
Analog comfort CI	24	93.13	68.00	100.00	9.68
TBUT TI	24	11.54	6.00	21.00	4.29
TBUT CI	24	10.92	7.00	19.00	2.87
Wettability TI	24	0.00	0.00	0.00	0.00
Wettability CI	24	0.00	0.00	0.00	0.00
Deposition TI	24	0.04	0.00	1.00	0.20
Deposition CI	24	0.08	0.00	2.00	0.41

TABLE 3 - Continued

Insertion	Valid N	Mean	Minimum	Maximum	Std. Dev.
1-Hour					
Movement TI	24	0.38	0.10	1.20	0.24
Movement CI	24	0.41	0.10	1.20	0.25
Inferior overlap TI	24	1.65	0.80	2.60	0.42
Inferior overlap CI	24	1.71	1.00	2.60	0.40
Decentration TI	24	0.19	0.00	0.35	0.12
Decentration CI	24	0.21	0.00	0.45	0.12
Analog comfort TI	24	94.46	70.00	99.00	7.52
Analog comfort CI	24	93.00	60.00	100.00	10.57
TBUT TI	24	10.58	5.00	19.00	3.86
TBUT CI	24	9.42	3.00	24.00	4.64
Wettability TI	24	0.00	0.00	0.00	0.00
Wettability CI	24	0.13	0.00	1.00	0.34
Deposition TI	24	0.13	0.00	1.00	0.34
Deposition CI	24	0.08	0.00	1.00	0.28

TI = Test Solution 1/PureVision lenses
CI = Control Opti-Free/PureVision lenses

The compositions of the present invention may be effectively used as multi-purpose no-rub contact lens solutions for removing and dispersing protein and lipid tear film deposits on both hard and soft-type contact lenses. For example, the subject compositions may be used when the wearer of contact lenses removes the contact lenses from the eyes. The contact lenses may be soaked in solutions of the present compositions at room temperature for a period ranging from about four to twelve hours. The lenses are then removed from the solution and replaced on the eyes. The wearer may optionally rinse the lenses in a preserved saline solution before replacing the lenses on the eyes.

When the cleaning process includes a rinsing step, however, the cleaning solution may contain higher concentrations of surfactant, e.g., 3 to 15 weight percent. However, the rinsing step may be omitted when, for example, the cleaning solution contains up to 1.5 weight percent of surfactant. In addition to the soaking method, the solutions disclosed herein are adaptable for use in equipment such as ultrasonic cleaners. Furthermore, because the solutions are also stable when heated to temperatures in the range of 80^0 to 90^0C, they are also adaptable for use with high temperature disinfecting methods. Typically, lenses are heated to 80^0 C in a disinfecting unit containing the solution for a time period of at least 10 minutes, removed and rinsed with isotonic saline.

While there is shown and described herein compositions for ophthalmic solutions, and methods of making and using the same, it will be manifest to those skilled in the art that various modifications may be made without departing from the spirit and scope of the underlying inventive concept. The present invention is likewise not intended to be limited to particular ophthalmic solutions or methods described herein except insofar as indicated by the scope of the appended claims.

We claim:

1. A composition comprising:

one or more polyethers;

one or more cationic polyelectrolytes;

one or more osmolality agents; and

a disinfecting amount of Alexidine, its salts, or a combination thereof.

2. A no-rub contact lens cleaning and disinfecting solution comprising:

one or more polyethers;

one or more cationic polyelectrolytes;

one or more osmolality agents; and

a disinfecting amount of Alexidine, its salts, or a combination thereof.

3. A no-rub contact lens cleaning and disinfecting solution that reduces or eliminates corneal or conjunctival staining comprising:

one or more polyethers to improve comfort of said contact lens for said contact lens wearer;

one or more cationic polyelectrolytes to control contact lens swelling;

one or more osmolality agents to improve in-eye solution comfort; and

a disinfecting amount of Alexidine, its salts, or a combination thereof.

4. A no-rub contact lens cleaning and disinfecting solution that reduces or eliminates wearer discomfort comprising:

one or more polyethers;

one or more cationic polyelectrolytes;

one or more osmolality agents; and

a disinfecting amount of Alexidine, its salts, or a combination thereof.

5. The composition of claim 1 wherein said one or more polyethers are selected from the group consisting of poloxamers, poloxamines and combinations thereof.

6. The composition of claim 1 wherein said one or more polyethers are present in an amount within the range of about 0.01 to about 15 weight percent.

7. The composition of claim 1 wherein said one or more cationic polyelectrolytes are selected from the group consisting of polyquaternium 1, polyquaternium 10, polyquaternium 11, polyquaternium 16, polyquaternium 44, polyquaternium 46 and combinations thereof.

8. The composition of claim 1 wherein said one or more cationic polyelectrolytes are present in an amount within the range of about 0.001 to about 5 weight percent.

9. The composition of claim 1 wherein said disinfecting amount is of Alexidine.

10. The composition of claim 1 wherein said disinfecting amount is of Alexidine, its salts or a combination thereof present in an amount within the range of about 0.00001 to about 0.5 weight percent and reduces or eliminates corneal staining.

11. The composition of claim 1 wherein said one or more osmolality agents are selected from the group consisting of metal halides, diols, polyols, saccharides, amino acids and combinations thereof.

12. The composition of claim 1 wherein said one or more osmolality agents are present in an amount within the range of about 0.01 to about 2.5 weight percent.

13. The composition of claim 1 wherein said one or more osmolality agents are present in a concentration sufficient to increase cleaning efficacy without adversely affecting antimicrobial efficacy.

14. The composition of claim 1 wherein said composition includes one or more buffering agents.

15. The composition of claim 1 wherein said composition includes one or more buffering agents in an amount effective in maintaining the pH of the composition within the range of about 6.5 to about 7.8.

16. The composition of claim 1 wherein said one or more buffering agents are present in an amount within the range of about 0.01 to about 2.5 weight percent.

17. A method of making the composition of claim 1 comprising:

combining one or more polyethers;

one or more cationic polyelectrolytes;

one or more osmolality agents; and

a disinfecting amount of Alexidine, its salts or a combination thereof.

18. A method of using the composition of claim 1 comprising:

soaking a contact lens in said composition for a period of time of about 4 to about 12 hours.

19. The solution of claim 2, 3 or 4 wherein said one or more polyethers are selected from the group consisting of poloxamers, poloxamines and combinations thereof.

20. The solution of claim 2, 3 or 4 wherein said one or more polyethers are present in an amount within the range of about 0.01 to about 15 weight percent.

21. The solution of claim 2, 3 or 4 wherein said one or more cationic polyelectrolytes are selected from the group consisting of polyquaternium 1, polyquaternium 10, polyquaternium 11, polyquaternium 16, polyquaternium 44, polyquaternium 46 and combinations thereof.

22. The solution of claim 2, 3 or 4 wherein said one or more cationic polyelectrolytes are present in an amount within the range of about 0.001 to about 5 weight percent.

23. The solution of claim 2, 3 or 4 wherein said disinfecting amount is of Alexidine.

24. The solution of claim 2, 3 or 4 wherein said disinfecting amount is of Alexidine, its salts or a combination thereof present in an amount within the range of about 0.00001 to about 0.5 weight percent with reduced or eliminated levels of corneal staining.

25. The solution of claim 2, 3 or 4 wherein said one or more osmolality agents are selected from the group consisting of metal halides, diols, polyols, saccharides, amino acids and combinations thereof.

26. The solution of claim 2, 3 or 4 wherein said one or more osmolality agents are present in an amount within the range of about 0.01 to about 2.5 weight percent.

27. The solution of claim 2, 3 or 4 wherein said one or more osmolality agents are present in a concentration sufficient to increase cleaning efficacy without adversely affecting antimicrobial activity.

28. The solution of claim 2, 3 or 4 wherein said composition includes one or more buffering agents.

29. The solution of claim 2, 3 or 4 wherein said composition includes one or more buffering agents in an amount effective in maintaining the pH of the solution within the range of about 6.5 to about 7.8.

30. The solution of claim 2, 3 or 4 wherein said one or more buffering agents are present in an amount within the range of about 0.01 to about 2.5 weight percent.

31. A method of making the solution of claim 2, 3 or 4 comprising:

combining one or more polyethers;

one or more cationic polyelectrolytes;

one or more osmolality agents; and

a disinfecting amount of Alexidine, its salts or a combination thereof.

32. A method of using the solution of claim 2, 3 or 4 comprising:

soaking a contact lens in said composition for a period of time of about 4 to about 12 hours.

33. The composition of claim 1 wherein said composition is useful as

an in-eye conditioning solution, an in-eye cleaning solution or an in-eye cleaning and conditioning solution.

34. The composition of claim 1 wherein said composition is useful as in-eye drops to condition a contact lens while worn in an eye.

35. The composition of claim 1 wherein said composition is useful as in-eye drops to condition and clean a contact lens while worn in an eye.

36. A composition comprising:

one or more polyethers;

one or more cationic polyelectrolytes;

one or more osmolality agents; and

a disinfecting amount of Alexidine or its salts.

37. The composition of claim 36 wherein said one or more polyethers are Tetronic 1107 and Pluronic F127.

38. The composition of claim 36 wherein said one or more cationic polyelectrolytes are polyquaternium 10.

39. The composition of claim 36 wherein said one or more osmolality agents are sodium chloride.

40. A composition comprising:

Tetronic 1107 and Pluronic F127;

polyquaternium 10;

sodium chloride; and

a disinfecting amount of Alexidine , its salts or a combination thereof.

AMENDED CLAIMS
[received by the International Bureau on 11 November 2004 (11.11.2004);
original claims 1-40 replaced by amended claims 1-26 (6 pages)]

1. A composition comprising:

one or more polyethers;

one or more cationic polyelectrolytes;

one or more osmolality agents; and

a disinfecting amount of a disinfectant consisting essentially of Alexidine, its salts, or a combination thereof.

2. A no-rub contact lens cleaning and disinfecting composition comprising:

one or more polyethers;

one or more cationic polyelectrolytes;

one or more osmolality agents; and

a disinfecting amount of a disinfectant consisting essentially of a non-polymeric bis(biguanide) including Alexidine, its salts, or a combination thereof.

3. A no-rub contact lens cleaning and disinfecting composition that reduces or eliminates corneal or conjunctival staining comprising:

one or more polyethers in an amount sufficient to improve comfort of said contact lens for said contact lens wearer;

one or more cationic polyelectrolytes in an amount sufficient to control contact lens swelling;

one or more osmolality agents in an amount sufficient to improve in-eye solution comfort; and

a disinfecting amount of Alexidine, its salts, or a combination thereof and a less than staining amount of other biguanides.

4. A no-rub contact lens cleaning and disinfecting composition that reduces or eliminates wearer discomfort comprising:

one or more polyethers;

a cationic polyelectrolyte including a polyquaternium polymer;

one or more osmolality agents; and

a disinfecting amount of a disinfectant consisting essentially of Alexidine, its salts, or a combination thereof.

5. A composition of any one of claims 1-4 wherein said one or more polyethers are selected from the group consisting of poloxamers, poloxamines and combinations thereof.

6. A composition of any one of claims 1-4 wherein said one or more polyethers are present in an amount within the range of about 0.01 to about 15 weight percent.

7. A composition of any one of claims 1-4 wherein said one or more cationic polyelectrolytes are selected from the group consisting of polyquaternium 1, polyquaternium 10, polyquaternium 11, polyquaternium 16, polyquaternium 44, polyquaternium 46 and combinations thereof.

8. A composition of any one of claims 1-4 wherein said one or more cationic polyelectrolytes are present in an amount within the range of about 0.001 to about 5 weight percent.

9. A composition of claims 1-4, wherein said cationic polyelectrolyte is polyquarternium-10.

10. A composition of any one of claims 1-4 wherein said disinfecting amount is of Alexidine, its salts or a combination thereof present in an amount within the range of about 0.00001 to about 0.5 weight percent and reduces or eliminates corneal staining.

11. A composition of any one of claims 1-4 wherein said one or more osmolality agents are selected from the group consisting of metal halides, diols, polyols, saccharides, amino acids and combinations thereof.

12. A composition of any one of claims 1-4 wherein said one or more osmolality agents are present in an amount within the range of about 0.01 to about 2.5 weight percent.

13. A composition of any one of claims 1-4 wherein said one or more osmolality agents are present in a concentration sufficient to increase cleaning efficacy without adversely affecting antimicrobial efficacy.

14. A composition of any one of claims 1-4 wherein said composition includes one or more buffering agents.

15. A composition of any one of claims 1-4 wherein said composition includes one or more buffering agents in an amount effective in maintaining the pH of the composition within the range of about 6.5 to about 7.8.

16. A compositions of any one of claims 1-4 wherein said one or more buffering agents are present in an amount within the range of about 0.01 to about 2.5 weight percent.

17. A method of making a composition for disinfecting and cleaning of contact lenses comprising:

combining one or more polyethers;

one or more cationic polyelectrolytes including polyquarternium-10;

one or more osmolality agents; and

a disinfecting amount of a biguanide consisting essentially of Alexidine, its salts or a combination thereof.

18. A method of using any one of the compositions of claims 1-4 comprising:

soaking a contact lens in said composition for a period of time of about 4 to about 12 hours.

19. A method of making any one of compositions of claims 1-4 comprising:

combining one or more polyethers;

one or more cationic polyelectrolytes;

one or more osmolality agents; and

a disinfecting amount of a preservative consisting essentially of Alexidine, its salts or a combination thereof.

20. A composition of any one of claims 1-4 wherein said composition is useful as

an in-eye conditioning solution, an in-eye cleaning solution or an in-eye cleaning and conditioning solution.

21. A composition of any one of claims 1-4 wherein said composition is useful as in-eye drops to condition a contact lens while worn in an eye.

22. A composition of any one of claims 1-4 wherein said composition is useful as in-eye drops to condition and clean a contact lens while worn in an eye.

23. A composition comprising:

one or more polyethers;

one or more cationic polyelectrolytes;

one or more osmolality agents; and

a disinfecting amount of Alexidine or its salts.

24. The composition of claim 23 wherein said one or more polyethers are Tetronic 1107 and Pluronic F127.

25. The composition of claim 23 wherein said one or more osmolality agents are sodium chloride.

26. A composition comprising:
Tetronic 1107 and Pluronic F127;
polyquaternium 10;
sodium chloride; and
a disinfecting amount of Alexidine , its salts or a combination thereof.

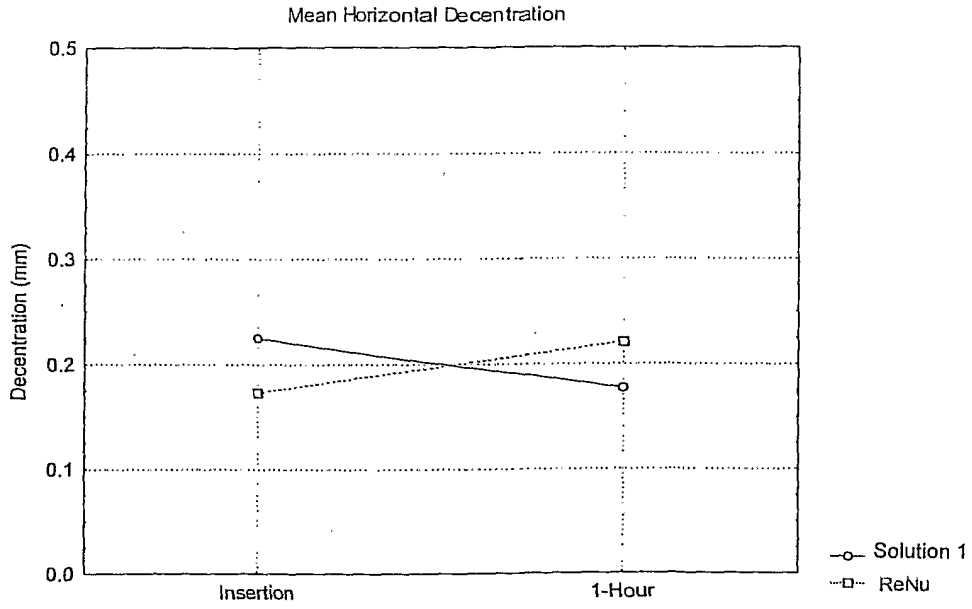
Mean Horizontal Decentration
Decentration (mm)
0.5
0.4
0.3
0.2
0.1
0.0
Insertion
1-Hour
Solution 1
ReNu

FIGURE *1/10*

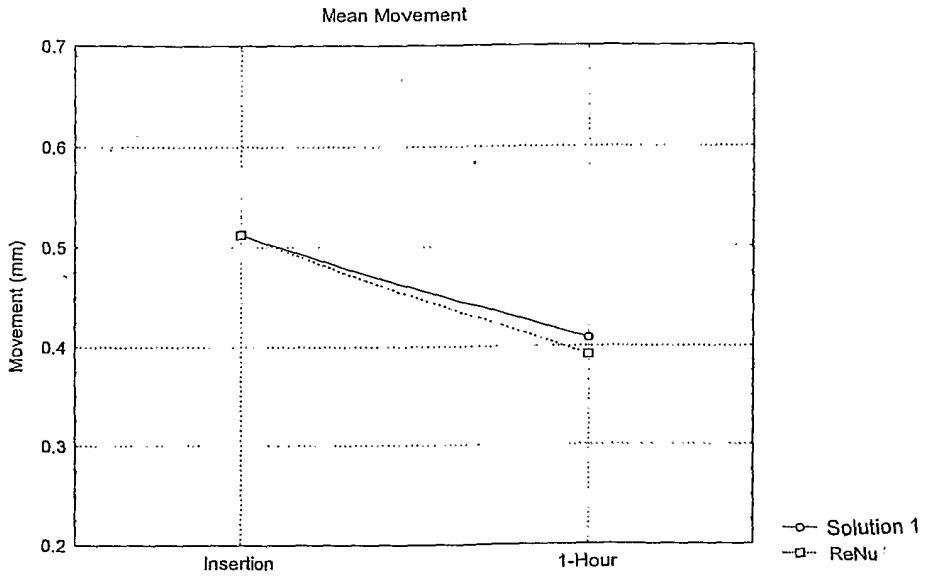
Mean Movement
0.7
0.6
0.5
0.4
0.3
0.2
Movement (mm)
Insertion
1-Hour
Solution 1
ReNu

FIGURE *2/10*

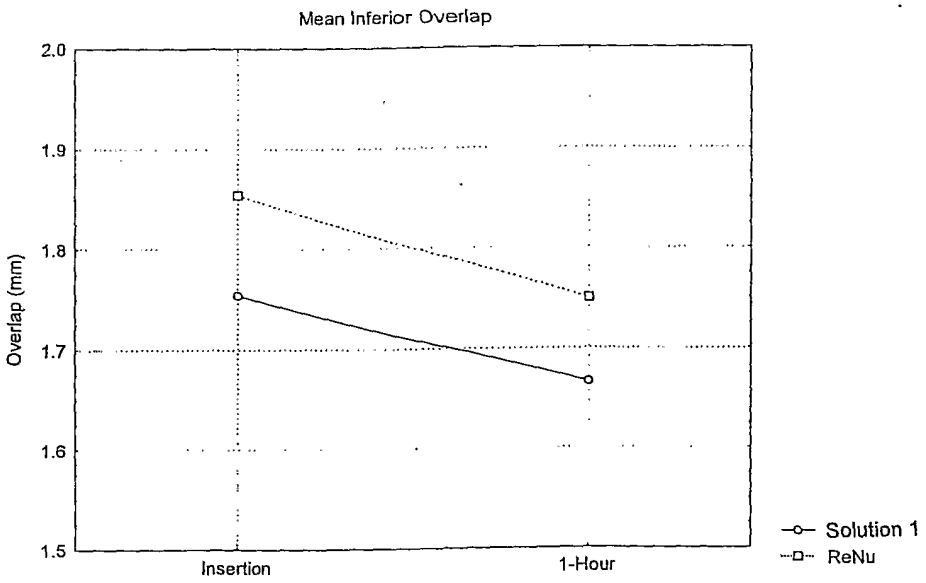
Mean Inferior Overlap
2.0
1.9
1.8
1.7
1.6
1.5
Overlap (mm)
Insertion
1-Hour
Solution 1
ReNu

FIGURE 3/10

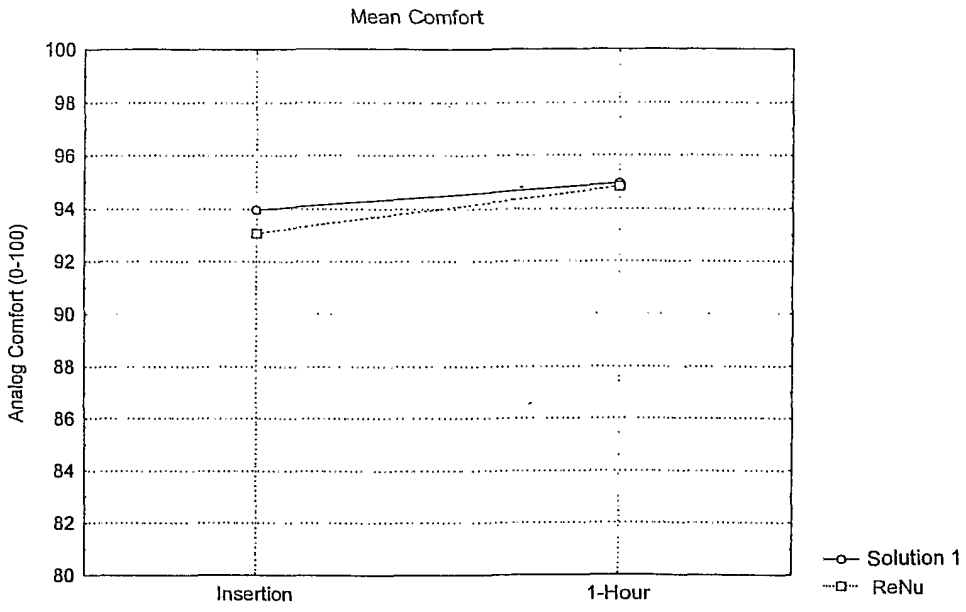
Mean Comfort
Analog Comfort (0-100)
100
98
96
94
92
90
88
86
84
82
80
Insertion
1-Hour
Solution 1
ReNu

FIGURE *4/10*

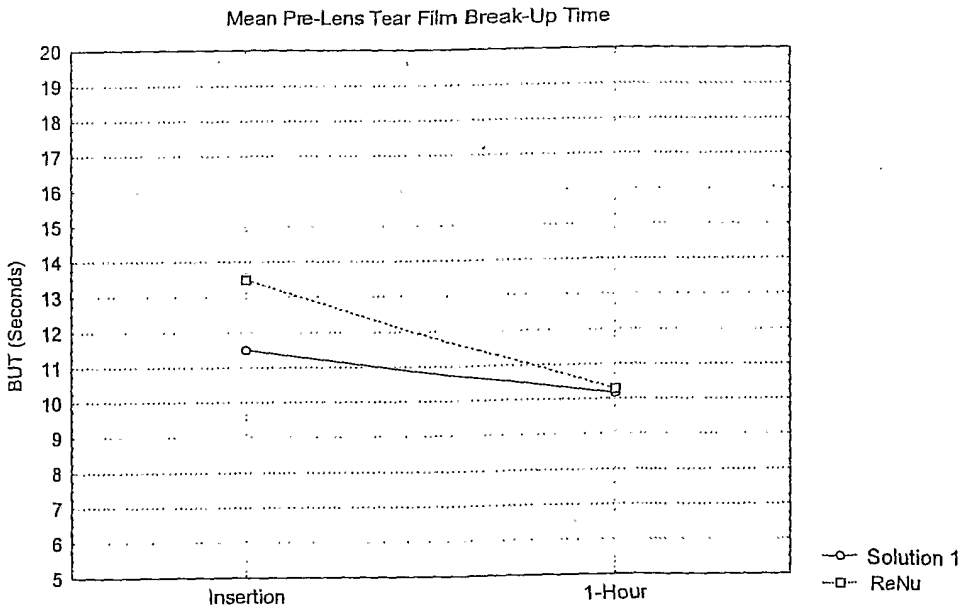
Mean Pre-Lens Tear Film Break-Up Time
BUT (Seconds)
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
Insertion
1-Hour
Solution 1
ReNu

FIGURE *5/10*

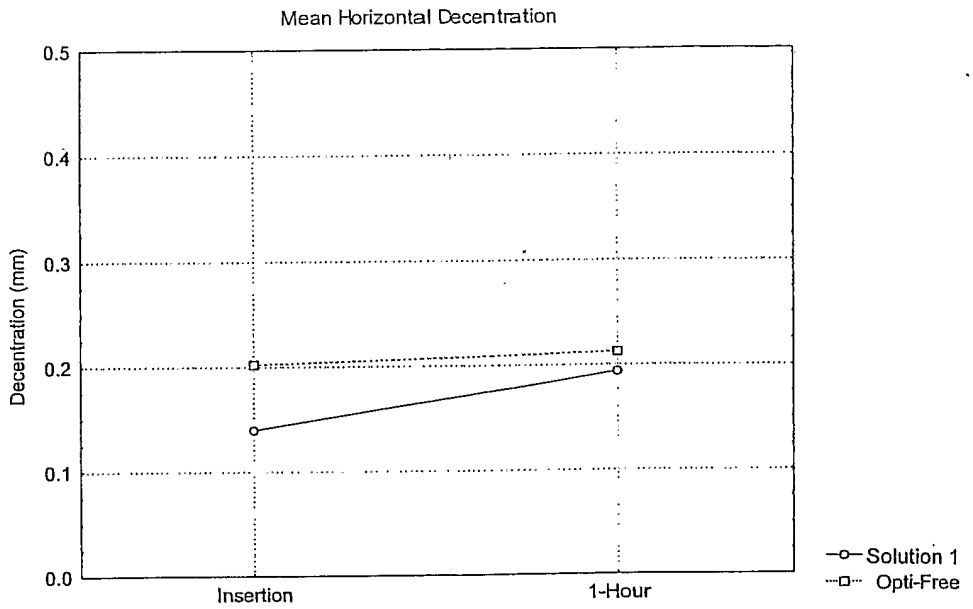
Mean Horizontal Decentration
Decentration (mm)
0.5
0.4
0.3
0.2
0.1
0.0
Insertion
1-Hour
Solution 1
Opti-Free

FIGURE *6/10*

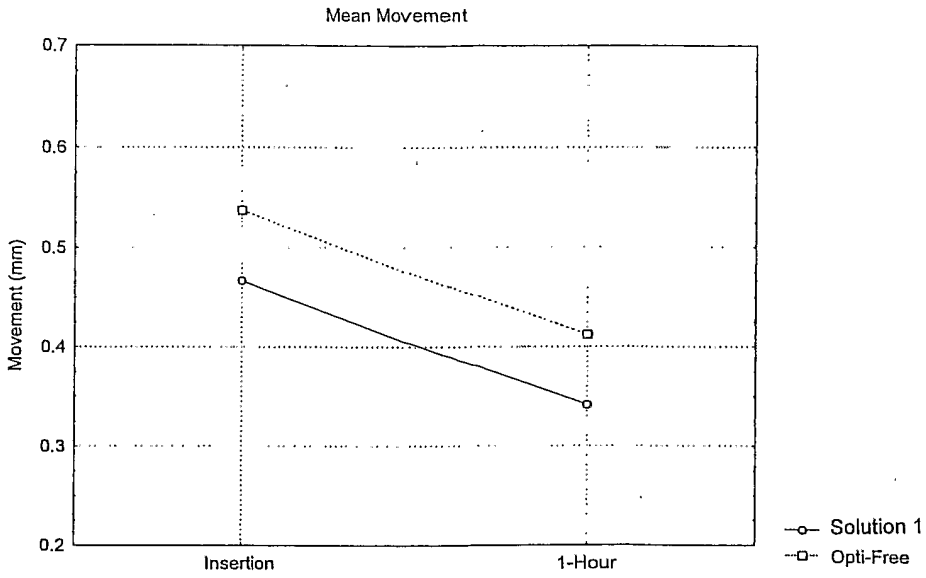
Mean Movement
Movement (mm)
0.7
0.6
0.5
0.4
0.3
0.2
Insertion
1-Hour
Solution 1
Opti-Free

FIGURE 7/10

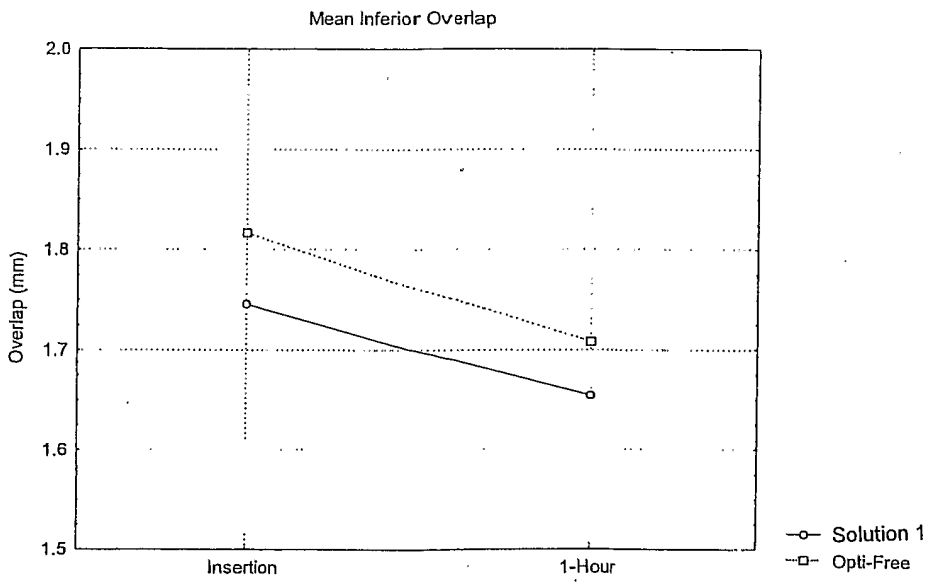
Mean Inferior Overlap
Overlap (mm)
2.0
1.9
1.8
1.7
1.6
1.5
Insertion
1-Hour
Solution 1
Opti-Free

FIGURE *8/10*

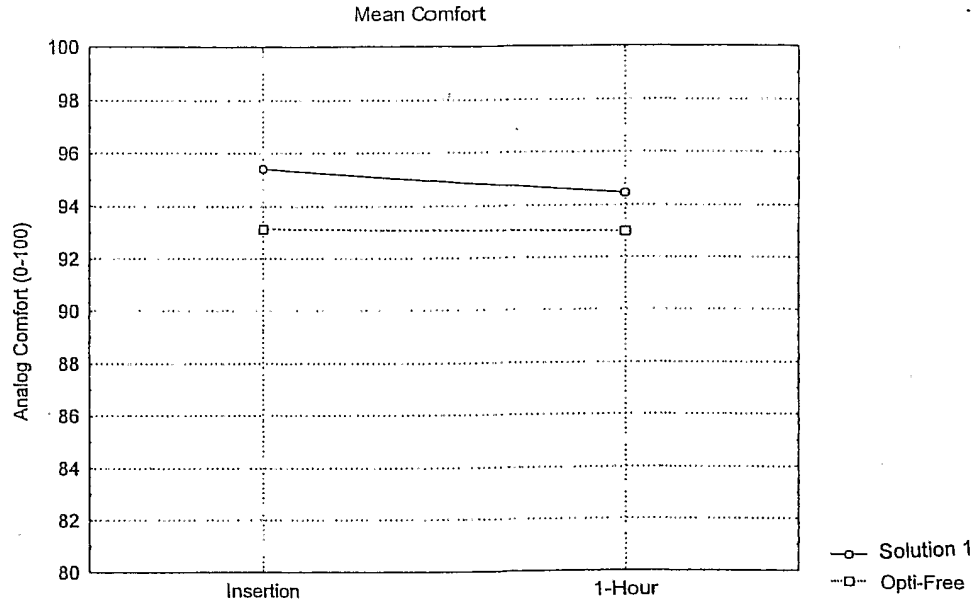
Mean Comfort
Analog Comfort (0-100)
100
98
96
94
92
90
88
86
84
82
80
Insertion
1-Hour
Solution 1
Opti-Free

FIGURE *9/10*

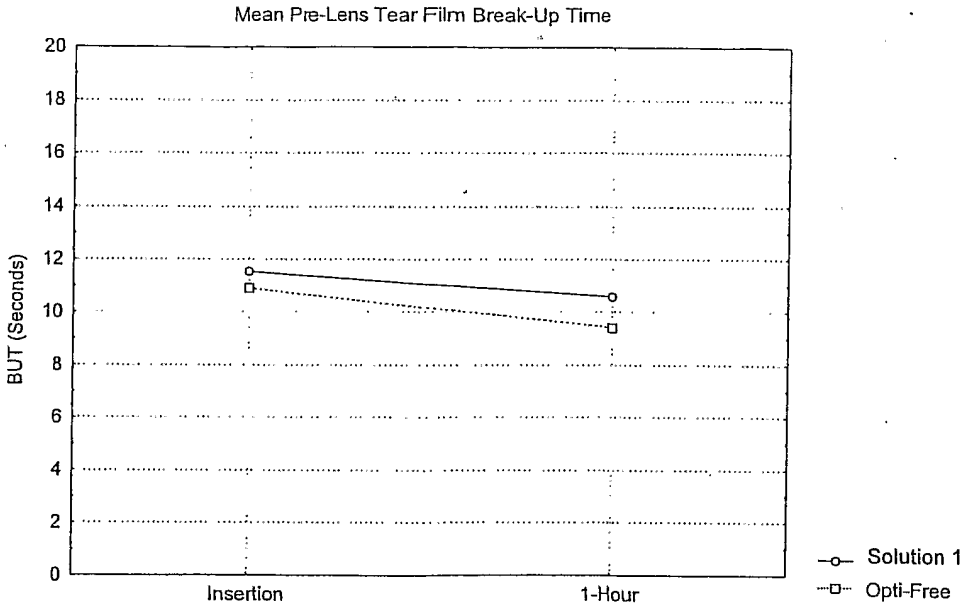
Mean Pre-Lens Tear Film Break-Up Time
BUT (Seconds)
20
18
16
14
12
10
8
6
4
2
0
Insertion
1-Hour
Solution 1
Opti-Free

FIGURE *10/10*

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/018377

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L12/14 C11D3/00 C11D1/66

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61L C11D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 369 112 B1 (XIA ERNING) 9 April 2002 (2002-04-09) column 9, line 64 - column 10, line 6 column 10, line 39 - column 11, line 3; claims 1,3-7,9,12	1-40
X	US 6 309 658 B1 (DENICK JR JOHN ET AL) 30 October 2001 (2001-10-30) column 3, lines 6-28 column 6, line 51 - column 8, line 9 column 9, lines 4-20 column 10, lines 20-52; claims 3,10,12,18	1-40

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
7 September 2004	14/09/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Jochheim, J

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/018377

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 965 088 A (LEVER ANDREA M ET AL) 12 October 1999 (1999-10-12) column 3, lines 31-42 column 8, lines 30-34 column 11, lines 25-35 column 12, line 61 - column 13, line 32 column 13, lines 53-64	1-40
X	WO 99/24542 A (BAUSCH & LOMB) 20 May 1999 (1999-05-20) page 3, lines 9-28 page 16, line 8 - page 18, line 7 page 18, line 20 - page 19, line 29	1-40
X	US 2003/096717 A1 (XIA ERNING ET AL) 22 May 2003 (2003-05-22) paragraphs '0002!, '0003!, '0010!, '0011!, '0024!, '0038!, '0039!, '0045!, '0048!, '0055! - '0058!	1-40

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2004/018377

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			JP	2001522672 T	20-11-2001
			WO	9924542 A1	20-05-1999
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			EP	1416976 A1	12-05-2004
			WO	03015835 A1	27-02-2003