



(43) International Publication Date  
31 August 2017 (31.08.2017)

WIPO | PCT

(10) International Publication Number  
**WO 2017/144874 A1**

- (51) International Patent Classification:  
*G02B 1/04* (2006.01) *C11D 1/66* (2006.01)
- (21) International Application Number:  
PCT/GB2017/050455
- (22) International Filing Date:  
22 February 2017 (22.02.2017)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
62/297,957 22 February 2016 (22.02.2016) US
- (71) Applicant: **COOPERVISION INTERNATIONAL HOLDING COMPANY, LP** [GB/BB]; Edghill House, Wildey Business Park, Suite 2, St. Michael (BB).
- (72) Inventors: **ROGERS, Victoria**; CooperVision, Inc., 5870 Stoneridge Drive, Suite 1, Pleasanton, California 94588 (US). **GEORGE, Melanie**; CooperVision, Inc., 5870 Stoneridge Drive, Suite 1, Pleasanton, California 94588 (US). **LUK, Andrew**; CooperVision, Inc., 5870 Stoneridge Drive, Suite 1, Pleasanton, ca 94588 (US).
- (74) Agent: **ABEL & IMRAY**; Westpoint Building, James Street West, Bath BA1 2DA (GB).

- (81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

**Published:**

— with international search report (Art. 21(3))

(54) Title: SILICONE HYDROGEL CONTACT LENSES HAVING IMPROVED LUBRICITY

(57) Abstract: Silicone hydrogel contact lenses are packaged in a packaging solution including an ophthalmically-acceptable concentration of a surfactant to provide a contact lens having a lower coefficient of friction compared to a control lens that is not packaged in the surfactant. The surfactant is a poly(ethylene oxide) (PEO)-containing surfactant having a molecular weight of up to about 6,000 daltons, or is an alkyl aryl-containing surfactant, or is both an alkyl aryl and PEO-containing surfactant having a molecular weight of up to about 6,000 daltons. Methods of manufacturing silicone hydrogel contact lenses are also described.



WO 2017/144874 A1

## **Silicone Hydrogel Contact Lenses Having Improved Lubricity**

### **FIELD**

[001] The field of the invention relates to silicone hydrogel contact lenses, packages containing silicone hydrogel contact lenses, and methods of manufacturing silicone hydrogel contact lenses.

### **BACKGROUND**

[001] Contact lenses made from silicone hydrogel materials are rapidly gaining popularity over contact lenses made from other materials because they are comfortable to wear and, unlike other hydrogel materials, have the added advantage of having high oxygen permeability, which is believed to be healthier for the eye compared to silicone-free hydrogel contact lenses. While silicone hydrogel contact lenses are typically highly lubricious and comfortable when initially worn, they often become less comfortable as wearing time progresses. This decreased discomfort may be due in part to changes in the physical properties of the surface of the contact lens. For example, many commercial contact lenses are packaged in packaging solutions that contain comfort polymers or wetting agents. However, during wear these comfort agents become washed away by the wearer's tears. Additionally, upon removal from its packaging solution and exposure to air, hydrophobic groups within the silicone hydrogel matrix may migrate toward the surface of the lens, resulting in non-wettable regions of the lens. There is a need for silicone hydrogel contact lenses that remain comfortable during the entire length of lens wearing time.

[002] Background publications include U.S. Pat. Appl. Publ. No. 2008/0110770, U.S. Pat. Appl. Publ. No. 2014/0102917, U.S. Pat. No. 6,440,366, U.S. Pat. No. 6,867,172, and U.S. Pat. No. 8,647,658.

## SUMMARY

**[003]** In one aspect, the invention provides an unworn sterile silicone hydrogel contact lens immersed in a packaging solution and sealed in a package, wherein the packaging solution comprises an ophthalmically-acceptable concentration of from about 0.01 wt.% up to about 0.5 wt.% of an alkyl aryl-containing surfactant (based on the total weight of the packaging solution). Advantageously, the silicone hydrogel contact lens has a lower coefficient of friction after an overnight wash compared to a control lens. In one example, the alkyl aryl-containing surfactant is tyloxapol. In a specific example, the contact lens has a lower surface concentration of silicon compared to a control lens, as determined by cold stage X-ray photoelectron spectroscopy (XPS).

**[004]** In another aspect, the invention provides an unworn sterile silicone hydrogel contact lens immersed in a packaging solution and sealed in a package, wherein the packaging solution comprises an ophthalmically-acceptable concentration of from about 0.01 wt.% up to about 0.5 wt.% of a poly(ethylene oxide) (PEO)-containing surfactant having a molecular weight of up to about 6,000 daltons. The silicone hydrogel contact lens advantageously has a lower coefficient of friction after an overnight wash compared to a control lens.

**[005]** Another aspect of the invention is a method of manufacturing a silicone hydrogel contact lens comprising curing a polymerizable composition comprising at least one silicone monomer and at least one hydrophilic monomer to form a polymeric lens body; packaging the polymeric lens body with a packaging solution comprising a surfactant, wherein the surfactant is a poly(ethylene oxide) (PEO)-containing surfactant having a molecular weight of up to about 6,000 daltons, or is an alkyl aryl-containing surfactant, or is a surfactant that is both alkyl aryl-containing and PEO-containing, or is a combination thereof; and heating the packaged polymeric lens body to provide an unworn, sterile packaged silicone hydrogel contact lens. In a specific example, the concentration of the surfactant in

the packaging solution is from about 0.01 wt.% up to about 0.5 wt.% prior to contact with the polymeric lens body.

**[006]** Another aspect of the invention is a contact lens package comprising a base member having a cavity for accommodating a packaging solution and a contact lens; a silicone hydrogel contact lens in the cavity of the base member; and a packaging solution in the cavity of the base member comprising from about 0.01wt% to about 0.1wt% tyloxapol. The silicone hydrogel contact lens can have a coefficient of friction less than 0.09 at a constant sliding speed of 0.5 mm/sec at a constant load of 0.5 g for 12 seconds at a temperature of about 20 to 25 degrees C.

## **DETAILED DESCRIPTION**

**[007]** Highly lubricious silicone hydrogel contact lenses and their method of manufacture are described herein. The silicone hydrogel contact lenses remain lubricious after prolonged wear, for example up to 8 or 10 hours of continuous wear or longer, providing a more comfortable contact lens wearing experience. The contact lens is provided in an aqueous packaging solution comprising an ophthalmically-acceptable concentration of from about 0.01 wt.% up to about 0.5 wt.% of a surfactant, wherein the surfactant is a poly(ethylene oxide) (PEO)-containing surfactant having a molecular weight of up to about 6,000 daltons, or is an alkyl aryl-containing surfactant, or is a surfactant that is both alkyl aryl-containing and PEO-containing, or is a combination thereof. As used herein, the term “weight percent” (wt.%) is intended to refer to the percentage of weight a particular ingredient contributes to a formulation. Thus, for example, when a wt.% is given for a surfactant, it is to be understood that this is based upon the total weight of the packaging solution that contains the surfactant. Further, references to a wt.% of a particular class of ingredient (e.g. surfactant) refers to the sum of the wt.% of all ingredients of the same type.

Thus for example, a packaging solution that comprises 0.1 wt.% of a first type of alkyl aryl-containing surfactant, and 0.2 wt.% of a second type of an alkyl aryl-containing surfactant is said to comprise 0.3 wt.% of an alkyl aryl-containing surfactant. The contact lens advantageously has a lower coefficient of friction after an overnight wash compared to a control lens. The term “coefficient of friction” refers to the kinetic (dynamic) coefficient of friction (CoF) of a contact lens as measured using a CETR Universal Micro-Tribometer (UMT) or equivalent using the method described in Example 1 or equivalent. As used herein, an “overnight wash” is one in which a lens is removed from its packaging solution and soaked in 4 mL PBS for approximately 15 hours at 20° C to 25° C (i.e. room temperature). In one example, the contact lens has a coefficient of friction that is at least 50% lower than that of the control lens. In various examples, the contact lens has a coefficient of friction that is at least 10%, 25%, or 50% and up to 99% lower than that of the control lens. In a further example, the control lens has a coefficient of friction (after overnight wash) of at least 0.5. In various examples, the control lens has a coefficient of friction of at least 0.25, 0.5 and up to about 1.0, 1.5, or 1.8. As used herein, a “control lens” refers to a contact lens that has not been contacted with the surfactant but is otherwise identical to the contact lens (i.e. test lens) to which it is being compared in that it was manufactured using the same contact lens formulation (referred to herein as a “polymerizable composition”), subjected to the same manufacturing processes, and subjected to the same overnight wash procedure prior to CoF measurement.

**[008]** As used herein, an alkyl aryl-containing surfactant refers to a surfactant comprising a hydrophobic portion containing at least one aryl group and at least one hydrocarbon chain of at least 2 carbon atoms. Each of the alkyl and aryl groups may be substituted or unsubstituted. In specific examples, the hydrocarbon chain comprises a chain of at least 2 or 3 carbon atoms and up to about 5, 10, 15 or 20 carbon atoms. In some examples, the

alkyl aryl-containing surfactant is an oligomer of another alkyl aryl-containing surfactant. For example, tyloxapol (CAS No. 25301-02-04) is an oligomer of the alkyl aryl-containing surfactant Triton X-100 (CAS No. 9002-93-1). As used herein, a PEO-containing surfactant refers to a surfactant comprising at least one poly(ethylene oxide) segment having the formula  $[-CH_2CH_2O]_n$  where n is an integer of at least 3. In various examples, n of the PEO segment is an integer of at least 3, 5 or 10, and up to about 25, 75 or 100. The surfactant may be nonionic or ionic (i.e. anionic, cationic, or zwitterionic). In a specific example, the surfactant is nonionic. In one example, the surfactant is both an alkyl aryl-containing and a polyethylene oxide-containing surfactant. In a specific example, the alkyl aryl-containing and polyethylene oxide-containing surfactant is tyloxapol, or a tocopheryl polyethylene glycol succinate (TPGS) (e.g. D- $\alpha$ -Tocopheryl polyethylene glycol 1000 succinate (CAS 9002-96-4), referred to herein as “TPGS-1000”), or a combination thereof. An additional advantage of tyloxapol and TPGS is that they exhibit antioxidant activity, which may be beneficial for ocular health.

**[009]** Without being limited by any particular theory, it is believed that the surfactants described herein may exert chaotropic activity, which changes the molecular structure of the silicone hydrogel matrix resulting in fewer hydrophobic silicone groups on the lens surface compared to a control lens. In some examples, the silicone hydrogel contact lens of the present invention has a surface concentration of elemental silicon that is at least 10% lower compared to a control lens. As used herein, surface concentration of silicon is determined by cold stage X-ray photoelectron spectroscopy (XPS) using the method described in Example 2 below, or equivalent method. In one example, the contact lens has a surface concentration of silicon that is at least 20% lower, at least 30% lower, or at least 40% lower than the surface concentration of silicone of a control lens.

[010] As used herein, an “ophthalmically-acceptable concentration” means a concentration of the surfactant in the packaging solution (prior to its contact with the contact lens) that does not exhibit cytotoxicity as determined by an ocular irritation study conducted in accordance with ISO 10993-10. An advantage of the surfactants used herein is that they are non-cytotoxic at concentrations effective at reducing surface concentration of silicon, and thus may be left in the final packaged contact lens. In contrast, other methods for reducing surface concentration of silicone of silicone hydrogel contact lenses employ toxic compounds that must be extracted from the contact lens prior to final packaging (see e.g. US Pat. Appln. Publ. No. 2014/0275434). Thus, the prior art method requires additional processing steps in order to provide an ophthalmically-acceptable contact lens, which add to manufacturing costs. Further, there is a desire to minimize the use of hazardous chemicals in manufacturing sites, which is another advantage of the present invention compared to the prior art. In specific examples, the concentration of the surfactant in the packaging solution prior to contact with the contact lens is from about 0.01 wt.% or 0.02 wt.%, up to about 0.05 wt.%, 0.075 wt.%, or 0.1 wt.%. Throughout this disclosure, when a series of lower limit ranges and a series of upper limit ranges are provided, all combinations of the provided ranges are contemplated as if each combination were specifically listed. For example, in the above listing of surfactant concentrations, all six possible concentration ranges are contemplated (i.e. 0.01 wt.% to 0.05 wt.%, 0.01 wt.% to 0.1 wt.%, etc. and 0.02 wt.% to 0.1 wt.%). Also, throughout this disclosure, when a series of values is presented with a qualifier preceding the first value, the qualifier is intended to implicitly precede each value in the series unless context dictates otherwise. For example, for the values listed above, it is intended that the qualifier “from about” implicitly precedes the values 0.02, and that the qualifier “up to about” implicitly precedes each of the values 0.075 and 0.1. In a specific example, the packaging solution comprises from about 0.01 wt.% to about 0.1 wt.% tyloxapol.

**[011]** In addition to the surfactant, the packaging solution typically comprises a buffered saline solution such as phosphate- or borate-buffered saline. The packaging solution may optionally contain additional ingredients such as a comfort agent, a hydrophilic polymer, an additive that prevents the lens from sticking to the container, and/or a chelating agent, etc. In some examples, the packaging solution is substantially free of polysaccharides (e.g. hyaluronic acid, hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxyethyl cellulose, etc.) or other high molecular weight polymers, such as polyvinyl pyrrolidone, which are commonly used as comfort polymers or thickening agents in ophthalmic solutions and contact lens packaging solutions. As used herein, a high molecular weight polymer refers to a polymer having an average molecular weight of at least 50,000 daltons.

**[012]** The PEO- or alkyl aryl-containing surfactant will typically have a molecular weight of less than about 6,000. In one example, the PEO- or alkyl aryl-containing surfactant has a molecular weight of less than about 5,000. The term “molecular weight” as used herein, refers to the absolute number average molecular weight (in units of daltons) of the surfactant as determined by <sup>1</sup>H NMR end-group analysis. In a specific example, the surfactant has a molecular weight of about 1,000 to about 5,000. In other examples, the surfactant has a molecular weight of at least 500, 750, or 1,000, up to about 4,000, 5,000, or 6,000. In a specific example, every ingredient of the packaging solution has a molecular weight less than 6,000 daltons.

**[013]** In various examples, the PEO- or alkyl aryl-containing surfactant has a hydrophilic-lipophilic balance (HLB) value that is at least 10, 11, or 12, up to about 14, 15, or 16, where the HLB value is calculated as twenty times the molecular weight of the hydrophilic portion of the polysiloxane divided by the total molecular weight of the polysiloxane. Both tyloxapol and TPGS-1000 have HLB values of about 13.



**[014]** The contact lens is provided unworn (i.e. it is a new contact lens, not having been previously used by a patient), immersed in the packaging solution and sealed in a package. The package may be a blister package, glass vial, or other appropriate container. The package comprises a base member having a cavity for accommodating a packaging solution and an unworn silicone hydrogel contact lens. The sealed package may be sterilized by sterilizing amounts of radiation, including heat or steam, such as by autoclaving, or by gamma radiation, e-beam radiation, ultraviolet radiation, etc. In a specific example, the packaged contact lens is sterilized by autoclaving. The final product is a sterile, packaged ophthalmically-acceptable contact lens. In a specific example, the invention provides a contact lens package, comprising a base member having a cavity for accommodating a packaging solution and a contact lens; an unworn silicone hydrogel contact lens in the cavity of the base member; and a packaging solution in the cavity of the base member, wherein the packaging solution comprises from about 0.01 wt.% to about 0.1 wt.% tyloxapol.

**[015]** Another aspect of the invention is a method of manufacturing an ophthalmically-acceptable silicone hydrogel contact lens. The method comprises curing a polymerizable composition comprising at least one silicone monomer and at least one hydrophilic monomer or hydrophilic polymer to form a polymeric lens body, and packaging the polymeric lens body with a packaging solution comprising a surfactant, wherein the surfactant is a poly(ethylene oxide) (PEO)-containing surfactant having a molecular weight of up to about 6,000 daltons, or is an alkyl aryl-containing surfactant, or is a surfactant that is both alkyl aryl-containing and PEO-containing, or is a combination thereof. The packaging solution has a concentration of the surfactant of from about 0.01% to about 0.1% prior to contact with polymeric lens body. The method further comprises heating (e.g. autoclaving) the packaged polymeric lens body to provide an unworn, sterile packaged contact lens

which advantageously has a lower coefficient of friction after an overnight wash compared to a control lens that has not been contacted with the surfactant but is otherwise identical.

**[016]** The polymerizable composition comprises at least one siloxane monomer and at least one hydrophilic monomer or at least one hydrophilic polymer, or a combination thereof. As used herein, the term “siloxane monomer” is a molecule that contains at least one Si-O group and at least one polymerizable group. Siloxane monomers useful in contact lens compositions are well-known in the art (see, e.g., US Pat No. 8,658,747 and US Pat No. 6,867,245). In some examples, the polymerizable composition comprises a total amount of siloxane monomer of at least 10 wt.%, 20 wt.%, or 30 wt.% up to about 40 wt.%, 50 wt.%, 60 wt.%, or 70 wt.%. Unless specified otherwise, as used herein, a given weight percentage (wt. %) of a component of the polymerizable composition is relative to the total weight of all polymerizable ingredients and IPN polymers (as described further below) in the polymerizable composition. The weight of the polymerizable composition contributed by components, such as diluents, that do not incorporate into the final contact lens product are not included in the wt.% calculation.

**[017]** In a specific example, the polymerizable composition comprises a hydrophilic vinyl monomer. As used-herein, a “hydrophilic vinyl monomer” is any siloxane-free (i.e. contains no Si-O groups) hydrophilic monomer having a polymerizable carbon-carbon double bond (i.e., a vinyl group) present in its molecular structure that is not part of an acryl group, where the carbon-carbon double bond of the vinyl group is less reactive than the carbon-carbon double bond present in a polymerizable methacrylate group under free radical polymerization. As used herein, the term “acryl group” refers to the polymerizable group present in acrylate, methacrylates, acrylamides, etc. Thus, while carbon-carbon double bonds are present in acrylate and methacrylate groups, as used herein, such polymerizable groups are not considered to be vinyl groups. Further, as used herein, a

monomer is “hydrophilic” if at least 50 grams of the monomer are fully soluble in 1 liter of water at 20°C (i.e., ~ 5% soluble in water) as determined visibly using a standard shake flask method. In various examples, the hydrophilic vinyl monomer is N-vinyl-N-methylacetamide (VMA), or N-vinyl pyrrolidone (NVP), or 1,4-butanediol vinyl ether (BVE), or ethylene glycol vinyl ether (EGVE), or diethylene glycol vinyl ether (DEGVE), or any combination thereof. In one example, the polymerizable composition comprises at least 10 wt.%, 15 wt.%, 20 wt.%, or 25 wt.% up to about 45 wt.%, 60 wt.%, or 75 wt.% of a hydrophilic vinyl monomer. As used herein, a given weight percentage of a particular class of component (e.g., hydrophilic vinyl monomer, siloxane monomer, or the like) in the polymerizable composition equals the sum of the wt.% of each ingredient in the composition that falls within the class. Thus, for example, a polymerizable composition that comprises 5 wt.% BVE and 25 wt.% NVP and no other hydrophilic vinyl monomer, is said to comprise 30 wt.% hydrophilic vinyl monomer. In one example, the hydrophilic vinyl monomer is a vinyl amide monomer. Exemplary hydrophilic vinyl amide monomers are VMA and NVP. In a specific example, the polymerizable composition comprises at least 25 wt.% of a vinyl amide monomer. In a further specific example, the polymerizable composition comprises from about 25 wt.% up to about 75 wt.% of VMA or NVP, or a combination thereof. Additional hydrophilic monomers that may be included in the polymerizable composition are N,N-dimethylacrylamide (DMA), 2-hydroxyethyl methacrylate (HEMA), ethoxyethyl methacrylamide (EOEMA), ethylene glycol methyl ether methacrylate (EGMA), and combinations thereof.

**[018]** In addition or as an alternative to a hydrophilic monomer, the polymerizable composition may comprise a non-polymerizable hydrophilic polymer, which results in a polymeric lens body comprising an interpenetrating polymer network (IPN) with the non-polymerizable hydrophilic polymer interpenetrating the silicone hydrogel polymer matrix.

In this example, the non-polymerizable hydrophilic polymer is referred to as an IPN polymer, which acts as an internal wetting agent in the contact lens. In contrast, polymer chains within the silicone hydrogel network that form by polymerization of monomers present in the polymerizable composition are not considered to be IPN polymers. The IPN polymer may be a high molecular weight hydrophilic polymer, for example from about 50,000 to about 500,000 daltons. In a specific example, the IPN polymer is polyvinylpyrrolidone (PVP). In other examples, the polymerizable composition is substantially free of polyvinyl pyrrolidone or other IPN polymer.

**[019]** The polymerizable composition may additionally comprise at least one cross-linking agent. As used herein, a “cross-linking agent” is a molecule having at least two polymerizable groups. Thus, a cross-linking agent can react with functional groups on two or more polymer chains so as to bridge one polymer to another. The cross-linking agent may comprise an acryl group or a vinyl group, or both an acryl group and a vinyl group. In certain examples, the cross-linking agent is free of siloxane moieties, i.e., it is a non-siloxane cross-linking agent. A variety of cross-linking agents suitable for use in silicone hydrogel polymerizable compositions are known in the field (see, e.g., U.S. Pat. No. 8,231,218, incorporated herein by reference). Examples of suitable cross-linking agents include, without limitation, lower alkylene glycol di(meth)acrylates such as triethylene glycol dimethacrylate and diethylene glycol dimethacrylate; poly(lower alkylene) glycol di(meth)acrylates; lower alkylene di(meth)acrylates; divinyl ethers such as triethyleneglycol divinyl ether, diethyleneglycol divinyl ether, 1,4-butanediol divinyl ether and 1,4-cyclohexanedimethanol divinyl ether; divinyl sulfone; di- and trivinylbenzene; trimethylolpropane tri(meth)acrylate; pentaerythritol tetra(meth)acrylate; bisphenol A di(meth)acrylate; methylenebis(meth)acrylamide; triallyl phthalate; 1,3-Bis(3-methacryloxypropyl)tetramethyldisiloxane; diallyl phthalate; and combinations thereof.

**[020]** As will be appreciated by those skilled in the art, the polymerizable composition may comprise additional polymerizable or non-polymerizable ingredients conventionally used in contact lens formulations such as one or more of a polymerization initiator, a UV absorbing agent, a tinting agent, an oxygen scavenger, a chain transfer agent, or the like. In some examples, the polymerizable composition may include an organic diluent in an amount to prevent or minimize phase separation between the hydrophilic and hydrophobic components of the polymerizable composition, so that an optically clear lens is obtained. Diluents commonly used in contact lens formulations include hexanol, ethanol, and/or other alcohols. In other examples, the polymerizable composition is free or substantially free (e.g., less than 500 ppm) of an organic diluent. In such examples, the use of siloxane monomers containing hydrophilic moieties such as polyethylene oxide groups, pendant hydroxyl groups, or other hydrophilic groups, may make it unnecessary to include a diluent in the polymerizable composition. Non-limiting examples of these and additional ingredients that may be included in the polymerizable composition are provided in U.S. Pat. No. 8,231,218.

**[021]** The polymerizable composition is dispensed into a contact lens mold and cured using conventional methods (e.g. thermal curing or UV-curing) to provide a polymeric lens body. The polymeric lens body is typically removed from the mold and washed, typically with alcohol and/or water, to remove unreacted components and hydrate the lens. The lens is then placed in a package with a volume of the packaging solution comprising the PEO- or alkyl aryl-containing surfactant, sealed, and heated (e.g. autoclaved). The packaging solution of the final product will have a concentration of the surfactant that is less than the concentration of the surfactant prior to the heating step. In a specific example, the packaging solution has a concentration of the surfactant that is at least 20% less than the concentration of the surfactant prior to the heating step.

[022] The following Examples illustrate certain aspects and advantages of the present invention, which should be understood not to be limited thereby.

**[023] Example 1: Surfactant Screening**

[024] Silicone hydrogel contact lenses designated “Lens-1” in Table 1 below, were prepared from a polymerizable composition similar to composition number 9 described in Table I of U.S. Pat. No. 8,614,261. The polymerizable composition comprised about 40 wt.% of a combination of NVP and VMA, about 55 wt.% of a combination of silicone monomers, as well as methacrylate-containing monomers, a cross-linking agent, and a polymerization initiator. The polymerizable composition was UV-cured in polar molds, and the resulting lens bodies were extracted in ethanol, and rinsed in water.

[025] Silicone hydrogel contact lenses designated “Lens-2” in Table 1 below, were prepared from a polymerizable composition similar to the compositions described in Example 2 of U.S. Pat. No. 9,164,298. The polymerizable composition comprised about 40 wt.% VMA, about 35 wt.% of a combination of silicone monomers, as well methacrylate-containing monomers, a cross-linking agent, and a polymerization initiator. The polymerizable composition was thermally-cured in non-polar molds, and the resulting lens bodies were extracted in ethanol, and rinsed in water.

[026] The contact lenses were soaked overnight in 3 mL of PBS with or without the commercially-available surfactant designated in Table 1 below. All surfactants were used at a concentration of 0.1 wt.%, except for coco betaine and PEG-7 glyceryl cocoate, which were used at a concentration of 0.5 wt.%. The lenses were removed from the surfactants and soaked in 4 mL PBS overnight at room temperature.

[027] The kinetic (dynamic) coefficient of friction (CoF) of the contact lenses were measured using a CETR Universal Micro-Tribometer (UMT) and CETR UMT Multi-

Specimen Testing System software, with a pin-on-disk sample mount at ambient temperature. An adhesive-backed, 2.5" round polyethylene terephthalate film was adhered to the rotational disk, which is mounted on the mounting ring of the UMT. Each contact lens was picked up with tweezers and mounted onto the sample holder. 100  $\mu$ L PBS was dispensed onto the PET substrate under the lens holder. The center of the lens on the pin tip was pressed against the PBS-wetted PET film moving at a constant sliding speed of 0.5 mm/sec at a constant load of 0.5 g for 12 seconds at a temperature between about 20 degrees C and 25 degrees C. CoF values were computed by the software, and the average values (n=3) for each lens is shown in Table 1.

**[028] Table 1: Surfactant Screening**

| Surfactant                                                 | Lens-1 CoF | Lens-2 CoF |
|------------------------------------------------------------|------------|------------|
| Control                                                    | 0.52       | 1.30       |
| Tyloxapol                                                  | 0.09       | 0.23       |
| Tetronic 1107                                              | 0.17       | 1.39       |
| Coco betaine                                               | 0.29       | 0.78       |
| PEG-7 glyceryl cocoate                                     | 0.09       | 0.75       |
| Zwittergent 3-10                                           | 0.98       | 1.08       |
| Poloxamer 407                                              | 0.18       | 0.33       |
| Tetronic 904                                               | 0.07       | 0.91       |
| Kolliphor P188                                             | 0.44       | 0.39       |
| Kolliphor RH 40                                            | 0.04       | 0.53       |
| Plantapon LGC Sorb                                         | 0.05       | 0.56       |
| Plantapon LC 7                                             | 0.05       | 0.37       |
| RLM-100                                                    | 0.03       | 0.08       |
| D- $\alpha$ -Tocopheryl polyethylene glycol 1000 succinate | 0.05       | 0.37       |

**[029]** Because of the low CoF values obtained for both lenses, tyloxapol and RLM-100 were evaluated further for use as a possible packaging solution additive. Titration studies showed that tyloxapol at a concentration of 0.02 wt.% remained effective in reducing CoF

of silicone hydrogel contact lenses after an overnight wash. A concentration of 0.035% tyloxapol in PBS was tested for cytotoxicity by an ocular irritation study in rabbits (ISO 10993-10), and was shown to be non-cytotoxic. In contrast, RLM-100 was cytotoxic at a concentration of 0.01 wt.%, and at this concentration was no longer effective in reducing CoF of the silicone hydrogel contact lenses.

**[030] Example 2: XPS Surface Analysis of Contact Lenses Packaged in 0.02 wt.% Tyloxapol.**

**[031]** Silicone hydrogel contact lenses were prepared from a polymerizable composition similar to the compositions described in Table I of U.S. Pat. No. 8,614,261. The polymerizable composition comprised about 40 wt.% of a combination of NVP and VMA, about 55 wt.% of a combination of silicone macromers, as well as methacrylate-containing monomers, a cross-linking agent, and a polymerization initiator. The polymerizable composition was UV-cured in polar molds, and the resulting lens bodies were extracted in ethanol, rinsed in water, sealed in blister packages containing about 1.8 ml PBS with or without 0.02wt% tyloxapol, and autoclaved.

**[032]** Two contact lenses (test-1, and test-2) that had been autoclaved in the tyloxapol-containing packaging solution and a control lens (packaged in PBS without tyloxapol) were tested by XPS. Each contact lens sample was rinsed in ultra-pure water three times for 2 minutes, 10 minutes, and then 2 minutes, with the volume of water replaced after each rinsing cycle. Each sample was mounted whole on a dome-shaped mount and placed in the intro chamber of a PHI 5802 Multitechnique XPS system. A droplet of ultra-pure water was placed on the center of the lens prior to freezing. Then the samples were frozen (using liquid nitrogen) in the intro chamber before the initial pumpdown (with nitrogen gas flow). The ice was sublimated while pumping down the intro chamber to preserve the hydrated



state of the surface. Once the ice was sublimated, the samples were introduced into the analytical chamber of the instrument. The spectral acquisitions were performed while the sample stage was constantly cooled by liquid nitrogen. The analytical parameters for the XPS analysis are shown in Table 2.

**[033] Table 2: Analytical Parameters**

|                                      |                                           |
|--------------------------------------|-------------------------------------------|
| <b>X-ray source</b>                  | Monochromatic Al K <sub>α</sub> s1486.6eV |
| <b>Acceptance Angle</b>              | ±23°                                      |
| <b>Take-off Angle</b>                | 45°                                       |
| <b>Analysis Area</b>                 | 800μm                                     |
| <b>Charge Correction</b>             | C-C, H, Si in C1s set to 284.8eV          |
| <b>Charge Compensation</b>           | Electron and Ion floods                   |
| <b>Cold Stage Sample Temperature</b> | −50°C... −100°C                           |

**[034]** The analysis depth ranged from about 50 Å to about 100 Å. The atomic concentrations of elements detected are shown in Table 3. The concentration values are normalized to 100% of the elements detected (XPS does not detect H).

**[035] Table 3: Atomic Concentrations (in %)**

| <b>Sample</b>  | <b>C1s</b> | <b>N1s</b> | <b>O1s</b> | <b>F1s</b> | <b>Si2p</b> |
|----------------|------------|------------|------------|------------|-------------|
| <b>Control</b> | 61.1       | 4.8        | 22.9       | 1.0        | 10.1        |
| <b>Test-1</b>  | 67.1       | 7.0        | 20.0       | 0.5        | 5.4         |
| <b>Test-2</b>  | 67.0       | 7.6        | 20.1       | 0.4        | 4.9         |

**[036] Example 3: Reduced Coefficient of Friction of Commercial Lenses Autoclaved in 0.02% Tyloxapol**

[037] Commercial contact lenses were removed from their original blisters and CoF was measured using the method described in Example 1. The lenses were then vortexed in 20 mL PBS three times, soaked overnight in 20 mL PBS, repackaged in 1.8 ml of either PBS (control) or PBS with 0.02wt% tyloxapol, and autoclaved. After autoclave, the Cof values of the repackaged contact lenses were measured. The results are shown in Table 4.

[038] **Table 4**

| Contact Lens |              | CoF     |         |           |
|--------------|--------------|---------|---------|-----------|
| Brand        | Material     | Blister | Control | Tyloxapol |
| Oasys        | senofilcon A | 0.05    | 1.31    | 0.09      |
| TruEye       | narafilcon A | 0.07    | 0.38    | 0.09      |
| Clariti      | somofilcon A | 0.14    | 2.45    | 0.15      |
| Biofinity    | comfilcon A  | 0.07    | 1.26    | 0.03      |
| MyDay        | stenfilcon A | 0.21    | 0.66    | 0.06      |

[039] The disclosure herein refers to certain illustrated examples, it is to be understood that these examples are presented by way of example and not by way of limitation. The intent of the foregoing detailed description, although discussing exemplary examples, is to be construed to cover all modifications, alternatives, and equivalents of the examples as may fall within the spirit and scope of the invention as defined by the additional disclosure.

[040] The entire contents of all cited references in this disclosure, to the extent that they are not inconsistent with the present disclosure, are incorporated herein by reference.

[041] Other embodiments of the present invention will be apparent to those skilled in the art from consideration of the present specification and practice of the present invention disclosed herein. It is intended that the present specification and examples be considered as exemplary only with a true scope and spirit of the invention being indicated by the following claims and equivalents thereof.

[042] The present invention includes the following aspects/embodiments/features in any order and/or in any combination:

1. An unworn sterile silicone hydrogel contact lens immersed in a packaging solution and sealed in a package, wherein the packaging solution comprises an ophthalmically-acceptable concentration of from about 0.01 wt.% up to about 0.5 wt.% of a surfactant (based on the total weight of the packaging solution), and wherein the surfactant is an alkyl aryl-containing surfactant or is a poly(ethylene oxide) (PEO)-containing surfactant having a molecular weight of up to about 6,000 daltons.
2. The contact lens of 1, wherein the surfactant is an alkyl aryl-containing surfactant.
3. The contact lens of 1, wherein the surfactant is a PEO-containing surfactant having a molecular weight of up to about 6,000 daltons.
4. The contact lens of any one of 1 to 3, having a lower coefficient of friction after an overnight wash compared to a control lens.
5. The contact lens of any one of 1 to 4, wherein the surfactant is an alkyl aryl polyethylene oxide.
6. The contact lens of any one of 1 to 4, wherein the surfactant is tyloxapol, or a tocopheryl polyethylene glycol succinate, or a combination thereof.
7. The contact lens of any one of 1 to 6, wherein the concentration of the surfactant is about 0.01 wt.% to about 0.1 wt.%, or about 0.01 wt.% to about 0.05 wt.%.
8. The contact lens of any one of 1 to 7, wherein the packaging solution is free of a high molecular weight polymer.
9. The contact lens of any one of 1 to 8, wherein every ingredient in the packaging solution has a molecular weight of less than 6,000 daltons.
10. The contact lens of any one of 1 to 9, wherein the surfactant has an HLB value of less than 16.

11. The contact lens of any one of 1 to 10, having a lower surface concentration of silicon compared to a control lens, wherein the surface concentration of silicon is determined by cold stage X-ray photoelectron spectroscopy (XPS).
12. The contact lens of any one of 1 to 11, wherein the surface concentration of silicon is at least 20% lower than a control lens.
13. The contact lens of any one of 1 to 4, wherein the surfactant is nonionic.
14. The contact lens of any one of 1 to 4, wherein the surfactant is ionic.
15. A method of manufacturing the contact lens of any one of 1 to 14, comprising curing a polymerizable composition comprising at least one silicone monomer and at least one hydrophilic monomer to form a polymeric lens body; packaging the polymeric lens body with the packaging solution comprising the surfactant; and heating the packaged polymeric lens body to provide an unworn, sterile packaged contact lens.
16. The method of 15, wherein the packaging solution has a concentration of the surfactant of from about 0.01 wt.% up to about 0.5 wt.% prior to contact with polymeric lens body.
17. The method of 15 or 16, wherein the concentration of the surfactant is from about 0.01% up to about 0.1% prior to contact with polymeric lens body.
18. The method of any one of 15 to 17, wherein the silicone hydrogel contact lens comprises a reaction product of a composition comprising a hydrophilic vinyl monomer.
19. The method of 18, wherein the hydrophilic vinyl monomer is selected from N-vinyl-N-methylacetamide (VMA), or N-vinyl pyrrolidone (NVP), or 1,4-butanediol vinyl ether (BVE), or ethylene glycol vinyl ether (EGVE), or diethylene glycol vinyl ether (DEGVE), or combinations thereof.
20. The method of any one of 15 to 19, wherein the polymerizable composition comprises at least 25 wt.% of a vinyl amide monomer.

21. The method of any one of 15 to 20, wherein the polymerizable composition is free of a polyvinyl pyrrolidone.
22. The method of any one of 15 to 21, wherein after the heating step, the packaging solution has a concentration of the surfactant that is at least 20% less than the concentration of the surfactant prior to contact with polymeric lens body.
23. A contact lens package comprising a base member having a cavity for accommodating a packaging solution and a contact lens; a silicone hydrogel contact lens in the cavity of the base member; and a packaging solution comprising a surfactant in the cavity of the base member, wherein the surfactant is an alkyl aryl-containing surfactant or is a poly(ethylene oxide) (PEO)-containing surfactant having a molecular weight of up to about 6,000 daltons.
24. The contact lens package of 23, wherein the contact lens and/or packaging solution has one or more features of the contact lens of 1 to 14 above.
25. The contact lens package of 23 or 24, wherein the packaging solution comprises from about 0.01 wt.% to about 0.1 wt.% tyloxapol.
26. The contact lens package of any one of 23 to 25, wherein the silicone hydrogel contact lens has a coefficient of friction less than 0.09 at a constant sliding speed of 0.5 mm/sec at a constant load of 0.5 g for 12 seconds at a temperature of about 20 to 25 degrees C.

**WHAT IS CLAIMED IS:**

1. An unworn sterile silicone hydrogel contact lens immersed in a packaging solution and sealed in a package, wherein the packaging solution comprises an ophthalmically-acceptable concentration of from about 0.01 wt.% up to about 0.5 wt.% of an alkyl aryl-containing surfactant, wherein the contact lens has a lower coefficient of friction after an overnight wash compared to a control lens that has not been contacted with the alkyl aryl-containing surfactant but is otherwise identical.
2. The contact lens of claim 1, wherein the alkyl aryl-containing surfactant comprises polyethylene oxide.
3. The contact lens of claim 1 or claim 2, wherein the alkyl aryl-containing surfactant has a molecular weight of up to about 6,000 daltons.
4. The contact lens of any preceding claim, wherein the alkyl aryl-containing surfactant has an HLB value of less than 16.
5. The contact lens of any preceding claim, wherein the alkyl aryl-containing surfactant is tyloxapol, or a tocopheryl polyethylene glycol succinate, or a combination thereof.
6. The contact lens of any preceding claim, wherein the concentration of the alkyl aryl-containing surfactant is about 0.01 wt.% to about 0.1 wt.%.
7. The contact lens of any preceding claim having a lower surface concentration of silicon compared to the control lens, wherein the surface concentration of silicon is determined by cold stage X-ray photoelectron spectroscopy (XPS).

8. The contact lens of any preceding claim, wherein the surface concentration of silicon is at least 20% lower than the control lens.
9. An unworn sterile silicone hydrogel contact lens immersed in a packaging solution and sealed in a package, wherein the packaging solution comprises from about 0.01 wt.% to about 0.1 wt.% tyloxapol, and wherein the contact lens has a lower coefficient of friction after an overnight wash compared to a control lens that has not been contacted with the tyloxapol but is otherwise identical.
10. A contact lens package comprising:
  - a base member having a cavity for accommodating a packaging solution and a contact lens;
  - an unworn silicone hydrogel contact lens in the cavity of the base member; and
  - a packaging solution in the cavity of the base member, wherein the packaging solution comprises from about 0.01 wt.% to about 0.1 wt.% tyloxapol.
11. The contact lens package of claim 10, wherein the silicone hydrogel contact lens comprises a reaction product of a composition comprising a hydrophilic vinyl monomer.
12. The contact lens package of claim 10, wherein the hydrophilic vinyl monomer is selected from N-vinyl-N-methylacetamide (VMA), or N-vinyl pyrrolidone (NVP), or 1,4-butanediol vinyl ether (BVE), or ethylene glycol vinyl ether (EGVE), or diethylene glycol vinyl ether (DEGVE), or combinations thereof.

13. The contact lens package of claim 10, wherein the silicone hydrogel contact lens comprises a reaction product of a polymerizable composition comprising at least 25 wt.% of a vinyl amide monomer.
14. The contact lens package of any one of claims 10 to 13, wherein the silicone hydrogel contact lens comprises a reaction product of a polymerizable composition that is free of a polyvinyl pyrrolidone.
15. The contact lens package of any one of claims 10 to 14, wherein the packaging solution is free of a high molecular weight polymer.
16. The contact lens package of any one of claims 10 to 15, wherein the silicone hydrogel contact lens has a coefficient of friction less than 0.09 at a constant sliding speed of 0.5 mm/sec at a constant load of 0.5 g for 12 seconds at a temperature of about 20 to 25 degrees C.
17. An unworn sterile silicone hydrogel contact lens immersed in a packaging solution and sealed in a package, wherein the packaging solution comprises an ophthalmically-acceptable concentration of from about 0.01 wt.% up to about 0.5 wt.% of a poly(ethylene oxide) (PEO)-containing surfactant having a molecular weight of up to about 6,000 daltons, wherein the contact lens has a lower coefficient of friction after an overnight wash compared to a control lens that has not been contacted with the PEO-containing surfactant but is otherwise identical.
18. The contact lens of claim 17, wherein the PEO-containing surfactant is an alkyl aryl polyethylene oxide.



19. The contact lens of claim 17 or claim 18, wherein the PEO-containing surfactant is tyloxapol, or a tocopheryl polyethylene glycol succinate, or a combination thereof.
20. The contact lens of any one of claims 17 to 19, wherein the concentration of the PEO-containing surfactant is about 0.01 wt.% to about 0.1 wt.%.
21. The contact lens of any one of claims 17 to 20, wherein the concentration of the PEO-containing surfactant is about 0.01 wt.% to about 0.05 wt.%.
22. The contact lens of any one of claims 17 to 21, wherein the packaging solution is free of a high molecular weight polymer.
23. The contact lens of any one of claims 17 to 22, wherein every ingredient in the packaging solution has a molecular weight of less than 6,000 daltons.
24. The contact lens of any one of claims 17 to 23, wherein the PEO-containing surfactant has an HLB value of less than 16.
25. The contact lens of any one of claims 17 to 24, having a lower surface concentration of silicon compared to the control lens, wherein the surface concentration of silicon is determined by cold stage X-ray photoelectron spectroscopy (XPS).
26. The contact lens of claim 25, wherein the surface concentration of silicon is at least 20% lower than the control lens.

27. A method of manufacturing an ophthalmically-acceptable silicone hydrogel contact lens comprising:

- a) curing a polymerizable composition comprising at least one silicone monomer and at least one hydrophilic monomer to form a polymeric lens body;
- b) packaging the polymeric lens body with a packaging solution comprising an alkyl aryl-containing surfactant, wherein the packaging solution has a concentration of the alkyl aryl-containing surfactant of from about 0.01 wt.% up to about 0.5 wt.% prior to contact with polymeric lens body; and
- c) heating the packaged polymeric lens body to provide an unworn, sterile packaged contact lens,

wherein the contact lens has a lower coefficient of friction after an overnight wash compared to a control lens that has not been contacted with the alkyl aryl-containing surfactant but is otherwise identical.

28. The method of claim 27, wherein the alkyl aryl-containing surfactant comprises polyethylene oxide.

29. The method of claim 27 or 28, wherein the alkyl aryl-containing surfactant has a molecular weight of up to about 6,000 daltons.

30. The method of any one of claims 27 to 29, wherein the alkyl aryl-containing surfactant has an HLB value of less than 16.

31. The method of any one of claims 27 to 30, wherein the alkyl aryl-containing surfactant is tyloxapol, or a tocopheryl polyethylene glycol succinate, or a combination thereof.

32. A method of manufacturing an ophthalmically-acceptable silicone hydrogel contact lens comprising:

- a) curing a polymerizable composition comprising at least one silicone monomer and at least one hydrophilic monomer to form a polymeric lens body;
- b) packaging the polymeric lens body with a packaging solution comprising a poly(ethylene oxide) (PEO)-containing surfactant having a molecular weight of up to about 6,000 daltons, wherein the packaging solution has a concentration of the PEO-containing surfactant of from about 0.01 wt.% up to about 0.5 wt.% prior to contact with polymeric lens body; and
- c) heating the packaged polymeric lens body to provide an unworn, sterile packaged contact lens,

wherein the contact lens has a lower coefficient of friction after an overnight wash compared to a control lens that has not been contacted with the PEO-containing surfactant but is otherwise identical.

33. The method of claim 32, wherein the concentration of the PEO-containing surfactant is from about 0.01 wt.% up to about 0.1 wt.% prior to contact with polymeric lens body.

34. The method of claim 32 or 33, wherein every ingredient in the packaging solution has a molecular weight of less than 6,000 daltons.

35. The method of any one of claims 32 to 34, wherein the PEO-containing surfactant has an HLB value of less than 16.

36. The method of any one of claims 32 to 35, wherein the polymerizable composition comprises N-vinyl-N-methylacetamide (VMA), or N-vinyl pyrrolidone (NVP), or a combination thereof.
37. The method of any one of claims 32 to 36, wherein the polymerizable composition comprises at least 25 wt.% of a vinyl amide monomer.
38. The method of any one of claims 32 to 37, wherein the polymerizable composition is free of a polyvinyl pyrrolidone.
39. The method of claims 32 to 38, wherein after the heating step, the packaging solution has a concentration of the PEO-containing surfactant that is at least 20% less than the concentration of the PEO-containing prior to contact with polymeric lens body.
40. The method of any one of claims 32 to 39, wherein the PEO-containing surfactant is tyloxapol.
41. The method of any one of claims 32 to 40, wherein the contact lens has a lower surface concentration of silicon compared to a control lens that has not been contacted with the PEO-containing surfactant but is otherwise identical, wherein surface concentration of silicon is determined by X-ray photoelectron spectroscopy (XPS).

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/GB2017/050455

A. CLASSIFICATION OF SUBJECT MATTER  
INV. G02B1/04 C11D1/66  
ADD.

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)  
G02B 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 practicable, search terms used)

EPO-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                                                                                               | Relevant to claim No. |
|-----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X         | US 2003/130144 A1 (ALVAREZ NAYIBY [US] ET AL) 10 July 2003 (2003-07-10)                                                                                                                                                                                                                                                                                                                                          | 1-41                  |
| Y         | concentration tyloxapol 1%;<br>example 1; tables 1-4; compound Solution A                                                                                                                                                                                                                                                                                                                                        | 1-41                  |
| Y         | -----<br>WO 98/55155 A2 (BAUSCH & LOMB [US];<br>SALPEKAR ANIL [US]; TONGE STEPHEN RONALD<br>[GB]) 10 December 1998 (1998-12-10)<br>same technical field: packaging solutions<br>for hydrogel contact lenses;<br>page 1, line 6 - line 8<br>0,025% tyloxapol; no SILICON hydrogel<br>contact lens;<br>page 21, line 7<br>0,5% tyloxapol; no SILICON hydrogel<br>contact lens;<br>page 22, line 5<br>-----<br>-/-- | 1-41                  |



Further documents are listed in the continuation of Box C.



See patent family annex.

\* Special categories of cited documents :

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

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"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

11 May 2017

Date of mailing of the international search report

22/05/2017

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040,  
Fax: (+31-70) 340-3016

Authorized officer

Stabel, Andreas

## INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2017/050455

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT |                                                                                                                                                                               |                       |
|------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Category*                                            | Citation of document, with indication, where appropriate, of the relevant passages                                                                                            | Relevant to claim No. |
| Y                                                    | WO 02/087326 A1 (ALLERGAN INC [US])<br>7 November 2002 (2002-11-07)<br>Multi-purpose contact lens solution<br>comprising vitamine E TPGS as surfactant;<br>example 1<br>----- | 5,19,31               |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2017/050455

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s)  | Publication<br>date     |
|-------------------------------------------|---------------------|-----------------------------|-------------------------|
| US 2003130144                             | A1                  | 10-07-2003                  | AR 041179 A1 04-05-2005 |
|                                           |                     | AU 2003268249 A1 29-03-2004 |                         |
|                                           |                     | BR 0314135 A 12-07-2005     |                         |
|                                           |                     | CA 2497841 A1 18-03-2004    |                         |
|                                           |                     | CN 1681538 A 12-10-2005     |                         |
|                                           |                     | DE 10393239 B4 04-08-2016   |                         |
|                                           |                     | DE 10393239 T5 01-09-2005   |                         |
|                                           |                     | GB 2408035 A 18-05-2005     |                         |
|                                           |                     | HK 1076059 A1 22-09-2006    |                         |
|                                           |                     | JP 4896399 B2 14-03-2012    |                         |
|                                           |                     | JP 2005538412 A 15-12-2005  |                         |
|                                           |                     | KR 20050057287 A 16-06-2005 |                         |
|                                           |                     | TW 200413398 A 01-08-2004   |                         |
|                                           |                     | US 2003130144 A1 10-07-2003 |                         |
|                                           |                     | WO 2004022114 A1 18-03-2004 |                         |
| WO 9855155                                | A2                  | 10-12-1998                  | AU 736214 B2 26-07-2001 |
|                                           |                     | BR 9809966 A 01-08-2000     |                         |
|                                           |                     | CA 2292513 A1 10-12-1998    |                         |
|                                           |                     | CN 1259054 A 05-07-2000     |                         |
|                                           |                     | DE 69807217 D1 19-09-2002   |                         |
|                                           |                     | DE 69807217 T2 28-05-2003   |                         |
|                                           |                     | EP 0986406 A2 22-03-2000    |                         |
|                                           |                     | ES 2182322 T3 01-03-2003    |                         |
|                                           |                     | HK 1028209 A1 30-05-2003    |                         |
|                                           |                     | ID 23920 A 25-05-2000       |                         |
|                                           |                     | ID 24847 A 24-08-2000       |                         |
|                                           |                     | JP 4402152 B2 20-01-2010    |                         |
|                                           |                     | JP 4409635 B2 03-02-2010    |                         |
|                                           |                     | JP 2002504238 A 05-02-2002  |                         |
|                                           |                     | JP 2008304944 A 18-12-2008  |                         |
|                                           |                     | KR 20010013403 A 26-02-2001 |                         |
|                                           |                     | US 6440366 B1 27-08-2002    |                         |
|                                           |                     | US 2003109390 A1 12-06-2003 |                         |
|                                           |                     | WO 9855155 A2 10-12-1998    |                         |
| WO 02087326                               | A1                  | 07-11-2002                  | BR 0209317 A 20-07-2004 |
|                                           |                     | CA 2446491 A1 07-11-2002    |                         |
|                                           |                     | EP 1383377 A1 28-01-2004    |                         |
|                                           |                     | JP 2005502392 A 27-01-2005  |                         |
|                                           |                     | US 2003068250 A1 10-04-2003 |                         |
|                                           |                     | WO 02087326 A1 07-11-2002   |                         |