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(72) **Inventeurs/Inventors:**
MALTSEVA, INNA, US;
MORRIS, CAROL ANN, US;
KHONG, KATHLEEN, US;
LUK, ANDREW, US

(73) **Propriétaire/Owner:**
COOPERVISION INTERNATIONAL HOLDING
COMPANY, LP, BB

(74) **Agent:** BORDEN LADNER GERVAIS LLP

(54) **Titre : PROTECTION DE LENTILLES DE CONTACT CONTRE UNE CONTAMINATION MICROBIENNE PROVOQUEE PAR LA MANIPULATION**

(54) **Title: PROTECTION OF CONTACT LENSES FROM MICROBIAL CONTAMINATION CAUSED BY HANDLING**

(57) **Abrégé/Abstract:**

A sealed contact lens package contains a sterile, unworn contact lens and a contact lens packaging solution comprising epsilon polylysine (ePLL). The ePLL protects the contact lens from microbial contamination caused by handling the lens when it is removed from its package.

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- (71) **Applicant:** COOPERVISION INTERNATIONAL HOLDING COMPANY, LP [GB/BB]; Edghill House, Wildey Business Park, Suite 2, St Michael (BB).
- (72) **Inventors:** MALTSEVA, Inna; c/o CooperVision, Inc., 5870 Stoneridge Drive, Suite 1, Pleasanton, California 94588 (US). MORRIS, Carol Ann; c/o CooperVision, Inc., 5870 Stoneridge Drive, Suite 1, Pleasanton, California 94588 (US). KHONG, Kathleen; c/o CooperVision, Inc., 5870 Stoneridge Drive, Suite 1, Pleasanton, California 94588 (US). LUK, Andrew; c/o CooperVision, Inc., 5870 Stoneridge Drive, Suite 1, Pleasanton, California 94588 (US).
- (74) **Agent:** FLETCHER, Matthew James Edwin; c/o Abel & Imray, 20 Red Lion Street, London, Greater London WC1R 4PQ (GB).
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(57) **Abstract:** A sealed contact lens package contains a sterile, unworn contact lens and a contact lens packaging solution comprising epsilon polylysine (εPLL). The εPLL protects the contact lens from microbial contamination caused by handling the lens when it is removed from its package.

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Protection of Contact Lenses from Microbial Contamination Caused by Handling

FIELD

[001] The field of the invention is contact lenses packages.

BACKGROUND

[002] Microbial contamination of contact lenses is a serious public health concern due to its implications in ocular infiltrates, infections and microbial keratitis. Studies have demonstrated that lens handling greatly increases the incidence of microbial contamination of lenses (see e.g. Szczotka-Flynn et al., *Eye Contact Lens* (2010) 36(2):116-29). Daily disposable contact lens wearers can be particularly at risk for contamination due to the non-compliant storage of contact lenses after use in their original packaging solution and subsequent reuse (Boost et al., *Optom Vis Sci* (2011) 88(12):1409-13).

[003] ϵ -polylysine is a homopolymer of about 25-35 residues of L-lysine in which the epsilon-amino and carboxyl groups of L-Lysine are linked. It is a naturally-occurring polymer produced by *Streptomyces* species. It has broad-spectrum antimicrobial activity and has been widely used as a food preservative in Japan and as an additive in a variety of consumer products. The use of ϵ -polylysine in contact lens care solutions has been described (see e.g. U.S. Pat. No. 6,187,264, and U.S. Pat. Publ. No. 2005/0074467). Antimicrobial hydrogels made from epsilon-poly-L-lysine-graft-methacrylamide have been reported (Zhou et al., *Biomaterials* 32 (2011) 2704-2712).

[004] Other background publications include co-pending U.S. Pat. Appl. No. 14/109,976, U.S. Pat. Publ. No. 2012/0074352, U.S. Pat. Publ. No. 2011/0071091, U.S. Pat. Publ. No. 2005/0074467, U.S. Pat. Publ. No. 2004/0135967, U.S. Pat. No. 4,168,112, U.S. Pat. No. 7,282,214, U.S. Pat. No. 7,402,318, EP Pat. No. 1328303B1, and PCT Publ. No. WO94/13774.

SUMMARY

[005] The invention provides a sealed contact lens package comprising a sterile, unworn contact lens and a contact lens packaging solution, said contact lens packaging solution

comprising epsilon polylysine (ϵ PLL), wherein the unworn contact lens exhibits reduced contamination from at least one microbe, wherein said reduced contamination is determined by a test where *Pseudomonas aeruginosa* (PA) introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in an identical contact lens packaging solution but without said ϵ PLL. In one aspect of the invention, in the test, the unworn contact lens results in less than a two log kill of PA compared to the control contact lens when tested after 24 hours incubation with 104 CFU PA using an in vitro bioactivity assay. In another aspect of the invention, the contact lens package comprises (a) a plastic base member comprising a cavity which retains a sterile, unworn contact lens and a contact lens packaging solution comprising epsilon polylysine (ϵ PLL); and (b) a resealable cover that forms a liquid-tight seal with the plastic base member.

DETAILED DESCRIPTION

[006] We demonstrate that the initial removal of contact lenses from their original sterile packaging can result in significant microbial contamination of the lenses, even when handled immediately after hand washing. We have found that the addition of epsilon polylysine (ϵ PLL) to the contact lens packaging solution can reduce or completely eliminate such lens-handling contamination. This protective effect does not require that the ϵ PLL be attached to the contact lens material. Thus, the present invention is advantageous in that it is applicable to any type of contact lens material. It is particularly advantageous in situations where prolonged contact of a wearer's eye with an antimicrobial agent is not desired or is unnecessary. Disclosed herein is a sealed contact lens package comprising a sterile, unworn contact lens and a contact lens packaging solution comprising epsilon polylysine (ϵ PLL) in an amount effective to reduce or completely eliminate microbial contamination introduced to the lens during its removal from the package. As used herein, "unworn" means that the contact lens has never been placed on an eye, and "sealed" means having a water-tight seal.

[007] With the present invention, a sealed contact lens package comprising a sterile, unworn contact lens and a contact lens packaging solution comprising epsilon polylysine (ϵ PLL) are provided. The unworn contact lens advantageously exhibits reduced

contamination from at least one microbe. For example, the unworn contact lens exhibits reduced contamination from at least one microbe compared to a control contact lens packaged in an identical contact lens packaging solution but without said ϵ PLL. In one aspect, the invention provides a sealed contact lens package comprising a sterile, unworn contact lens and a contact lens packaging solution, said contact lens packaging solution comprising epsilon polylysine (ϵ PLL), wherein the unworn contact lens has anti-microbial activity on removal from the contact lens package. Advantageously, following removal from the contact lens package, the unworn contact lens having anti-microbial activity exhibits reduced contamination from at least one microbe. The reduced contamination and/or anti-microbial activity can be determined by a test where at least one microbe, such as *Pseudomonas aeruginosa* (PA), introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in an identical contact lens packaging solution but without said ϵ PLL. In the present invention, at least one microbe can comprise, consists of, consists essentially of, or include *Pseudomonas aeruginosa* and/or *Staphylococcus aureus*, and/or the at least one microbe is a microbe(s) found in microbial keratitis and/or at least one microbe causing at least in part or entirely ocular infiltrates and/or infections. The anti-microbial activity may, for example, be determined, in the test in which the unworn contact lens results in less than a two log kill of PA compared to the control contact lens when tested after 24 hours incubation with 10⁴ CFU PA using an in vitro bioactivity assay.

[008] The contact lens sealed in the contact lens package of the present disclosure may be made from any contact lens material, including but not limited to conventional hydrogels and silicone hydrogels. As used herein, a “conventional hydrogel” refers to a material formed from polymerization of one or more hydrophilic monomers such as 2-hydroxyethyl methacrylate (HEMA) or vinyl alcohol, optionally in combination with other monomers, and contains no siloxane (i.e. a molecule comprising at least one Si-O group). Examples of conventional hydrogels include etafilcon A, nelfilcon A, ocufilcon B, ocufilcon D, omafilcon A, omafilcon D and polymacon. Silicone hydrogel materials are typically formed from polymerization of one or more monomers or prepolymers comprising at least one Si-O group with one or more hydrophilic monomers. Examples of silicone hydrogels include balafilcon A, comfilcon A, enfilcon A, somofilcon A,

narafilecon A, narafilecon B, lotrafilecon A, stenfilecon A, and senofilecon A. In a specific example, the sealed contact lens package comprises a sterile, unworn silicone hydrogel contact lens. In a specific example, the silicone hydrogel contact lens is non-ionic, meaning it that it contains no anionic groups that bind to the cationic amine groups present in the ϵ PLL via ionic interaction. In a further specific example, the silicone hydrogel contact lens is made from a material selected from comfilecon A or stenfilecon A. In another example, the sealed contact lens package comprises an unworn conventional hydrogel contact lens made from a material selected from ocufilcon B, ocufilcon D, or omafilecon A.

[009] The contact lens sealed in the contact lens package of the present disclosure may be of any lens wear modality. Lens wear modality refers to the how many days and nights in a row the lens can be worn without removal. In one example, the contact lens sealed in the contact lens package of the present disclosure is a daily disposable lens. Daily disposable lenses are indicated for single use, up to about 12 or 16 hours of continuous wear, and should be discarded after the single use. In another example, the contact lens sealed in the contact lens package of the present disclosure is a daily wear lens. Daily wear lenses are worn during the waking hours, typically up to about 12 to 16 hours, and are removed before sleep. Daily wear lenses are typically stored in a contact lens case containing a contact lens care solution for cleaning and disinfecting the lens during the hours of non-use. Daily wear lenses are typically discarded after a maximum of 30 days wear. In yet another example, the contact lens is an extended wear lens. Extended wear lenses are typically worn continuously for up to 6, 14 or 30 consecutive days and nights.

[010] The packaging solution sealed within the contact lens package of the present disclosure may be any contact-lens compatible solution comprising an effective amount of ϵ PLL. In one example, the packaging solution comprises, consists, or consists essentially, of an aqueous solution of a buffer, and/or a tonicity agent, and ϵ PLL. In another example, the packaging solution contains additional agents such as one or more additional antimicrobial agents, and/or a comfort agent, and/or a hydrophilic polymer, and/or a surfactant and/or other additive that prevents the lens from sticking to the package. The packaging solution can have a pH in the range of about 6.8 or 7.0 up to about 7.8 or 8.0.

In one example, the packaging solution comprises phosphate buffer or borate buffer. In another example, the packaging solution comprises a tonicity agent selected from sodium chloride or sorbitol in an amount to maintain osmolality in the range of about 200 to 400 mOsm/kg, and typically from about 270 mOsm/kg up to about 310 mOsm/kg. Throughout this disclosure a reference to “examples”, “an example”, “one example”, or similar phrase, is intended to introduce a feature or features of the contact lens package, unworn contact lens, or packaging solution, as the case may be (depending on context) that can be combined with any combination of previously-described or subsequently-described examples (i.e. features), unless a particular combination of features is mutually exclusive, or if context indicates otherwise.

[011] An effective amount of εPLL is an amount that reduces microbial contamination introduced to the lens during its removal from the contact lens package (e.g., as compared to no εPLL present). The ability of εPLL to reduce microbial contamination introduced to a lens during its removal from a package can be demonstrated using methodology substantially as described in Example 1 or Example 2 below. Example 1 demonstrates that microbial contamination of contact lenses caused by normal, non-pathogenic skin flora can be significantly reduced by inclusion of εPLL in the contact lens packaging solution. Example 2 demonstrates that microbial contamination of contact lenses caused by *Pseudomonas aeruginosa* (PA), one of the most common pathogens implicated in microbial keratitis, can also be significantly reduced by inclusion of εPLL in the contact lens packaging solution. In a specific example, the unworn contact lens exhibits reduced contamination from PA introduced to the lens during removal from the packaging solution compared to a control contact lens in the same packaging comprising a contact lens packaging solution without εPLL but otherwise identical, as determined using a lens handling assay as described or substantially as described in Example 2. In various examples, the packaging solution comprises εPLL in amounts of at least 5 ppm, 10 ppm, 25 ppm, 50 ppm, 100 ppm, 150 ppm, 200 ppm, 250 ppm, or 500 ppm. In specific examples, the packaging solution comprises 10-50 ppm εPLL, 25-75 ppm εPLL, 50-150 ppm εPLL, or 100-500 ppm εPLL. The concentration of εPLL in a packaging solution is determined prior to its contact with the unworn contact lens.

[012] εPLL is commercially available typically as a homopolymer ranging from about 25 to about 35 lysine (LYS) residues (CAS no. 28211-04-3). All fractions of the naturally-occurring homopolymer of εPLL may be used. Alternatively, a select fraction of the εPLL may be used (e.g. a homopolymer of 30-35 LYS residues) with the remaining fractions removed and not used in this option. As an alternative to naturally-occurring εPLL, the εPLL used in the packaging solution may be obtained from synthetic peptide methods.

[013] In some examples the amount of εPLL included in the contact lens packaging solution results in less than a two log kill of PA compared to a control contact lens when tested after 24 hours incubation with 10^4 CFU (colony-forming units) PA as determined using an *in vitro* bioactivity assay substantially as described in Example 4 below. Optionally, the amount of εPLL included in the contact lens packaging solution results in the contact lens of the invention having a log kill of PA compared to a control contact lens of from 0.05 to 1.95, such as from 0.10 to 1.90. The amount of εPLL included in the contact lens packaging solution may, for example, result in a log kill of PA compared to a control contact lens of from 0.05 to 1.5, such as from 0.1 to 1.0. In such examples the contact lens package remains effective against microbial contamination introduced from initial handling of the lens during its removal from its original packaging, and thus is particularly suitable for a daily disposable contact lens.

[014] We demonstrate in Example 2 below that once the unworn contact lens is removed from the contact lens package the remaining packaging solution when covered up by the original blister foil can resist microbial contamination when left at ambient temperature for up to 16 hours. Thus, the contact lens package described herein can provide protection against microbial contamination that might arise from a non-compliant daily lens wearer who stores a worn lens overnight in its original package and remaining packaging solution for a second day of wear. Thus, in one example, the contact lens package comprises a plastic base member comprising a cavity configured to retain the contact lens and packaging solution and a flange region extending outwardly around the cavity. A removable foil is attached to the flange region to provide a sealed contact lens package. Such contact lens packages, which are commonly referred to as “blister packs”, are well-known in the art (see e.g. U.S. Pat. No. 7,426,993). In other examples, the contact lens

package comprises a contact lens indicated for daily wear for at least 2 days, wherein the package is configured to allow resealing after its initial opening for subsequent replacement of the lens for overnight storage after it has been worn. For example, the contact lens package may comprise a plastic base member comprising a cavity configured to retain the contact lens and packaging solution and a resealable cover. As used herein, a "resealable cover" is one that is configured to form a liquid-tight or spill-proof seal with the base member after the contact lens package is opened. For example, the plastic base member may comprise a plurality of threads for engagement with a compatible set of threads on a cap which serves as the resealable cover. Such configurations are commonly used in contact lens care cases (see e.g. U.S. Patent No. 3,977,517). Thus an advantage of the contact lens package disclosed herein is that it can serve a dual purpose, i.e. both as a contact lens package for a sterile, unworn contact lens and as a subsequent contact lens carrying case for a worn lens.

[015] It will be appreciated that conventional manufacturing methods can be used to manufacture the sealed contact lens package of any of the above examples. Thus, in one aspect of the present disclosure is a method of manufacturing a contact lens package including the step of placing an unworn contact lens and a contact lens packaging solution comprising ϵ PLL in a receptacle, placing a cover on the receptacle, and sealing the cover on the receptacle. Generally, the receptacle is configured to receive a single contact lens and an amount of packaging solution sufficient to completely cover the contact lens, typically about 0.5-1.5 ml. The receptacle may be made from any suitable material, such as glass or plastic. In one example, the receptacle comprises a plastic base member comprising a cavity configured to retain the contact lens and packaging solution and a flange region extending outwardly around the cavity, and the cover comprises a removable foil attached to the flange region to provide the sealed contact lens package. The removable foil may be sealed by any conventional means such as heat sealing or gluing. In another example, the receptacle is in the form of a plastic base member comprising a plurality of threads and the cover comprises a plastic cap member comprising a compatible set of thread for engagement with the threads of the base member thereby providing a resealable cover. It will be appreciated that other types of packaging can also be used to provide a resealable package. For example the contact lens package may comprise a

plastic cover comprising features that engage with compatible features of the receptacle to form an interference fit. The method of manufacturing the sealed contact lens package may further comprise sterilizing the unworn contact lens by autoclaving the sealed contact lens package.

[016] The details of the contact lens or lenses, components of the solution, formulations, and all of the various other details as described U.S. Patent Application No. 14/109,976, filed December 18, 2013 and entitled “Antimicrobial Ophthalmic Devices” are incorporated in their entirety by reference herein and form a part of the present application.

EXAMPLES

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

[018] Example 1: Contamination of commercial contact lenses after handling with washed hands

[019] Commercially available balafilcon A contact lenses in their original blister packaging were used in this lens-handling study. Five individuals washed their hands with soap and water and dried their hands using paper towels. The foil cover of each blister was opened aseptically with a gloved hand by the investigator. Each individual removed and gently rubbed the lens for approximately 5 seconds using the same hand used to turn off the faucet. Each rubbed lens was then placed into an individual sterile 2mL microcentrifuge (Eppendorf™) tube with 1mL PBS-T and capped. As used herein, PBS refers phosphate buffered saline of 0.78 wt.% NaCl, 0.05 wt.% sodium phosphate monobasic, and 0.36 wt.% sodium phosphate dibasic at pH 7.5. PBS-T refers to PBS with 0.05% Polysorbate 80.

[020] To extract any bacteria from the handled lenses, the tubes were sonicated for 3 cycles of 30 seconds each with 10 seconds vortexing in between. After the final sonication the tubes were vortexed for 10 minutes at 1000 rpm using a multi-tube vortexer. The entire volume of extract from each tube was plated onto a blood agar plate, allowed to

dry in a biochemical hood, and incubated at 37°C for 48-72 hours. Bacteria were counted and reported as CFU/lens. Each bacterium with a distinct phenotype was identified using a Biotyper.

[021] Detectable levels of contamination from common skin bacteria (*Staphylococcus epidermidis* and *Staphylococcus warneri*) were found on all five balafilcon A contact lenses. The range of contamination was from 115-6500 CFU/lens. No lens was sterile. Although the identified bacteria are not commonly found in microbial keratitis, they can cause disease in immune-compromised patients.

[022] To determine whether ϵ PLL in a contact lens packaging solution would be protective immediately against microbes deposited during lens removal from a blister package, the above lens-handling study was repeated using ocufilecon D, comfilecon A, and omafilecon A contact lenses that had been individually packaged in a contact lens blister package containing a packaging solution of either PBS or PBS with 500 ppm ϵ PLL, sealed with a foil cover, and autoclaved. All three lenses demonstrated a significant reduction in bioburden when ϵ PLL was present in the packaging solution, with the following average log kill: ocufilecon D - 2.4, comfilecon A - 1.4, and omafilecon A - 2.2.

[023] Finally, we repeated the above lens-handling study to compare the contamination level of an ocufilecon D contact lens removed from a sealed autoclaved package containing PBS packaging solution with or without 500 ppm ϵ PLL. We also determined the level of microbial contamination of ocufilecon D contact lenses that were removed from their sealed autoclaved packages containing PBS packaging solution. The lenses were removed from their packages aseptically using sterile forceps and placed into a well of a 24-well plate containing 1 ml of Optifree™ or AQuify™ brand contact lens solutions. Lenses exposed to ClearCare™ brand contact lens solutions were placed into the manufacturer-provided lens holder. After an overnight soak, the lenses (5 for each lens solution) were removed from the care solution using the above hand-washing, handling protocol and extracted as described above. As expected, the ClearCare™ contact lens solution, which does not contain any antimicrobial agents, did not provide protection against handling contamination. However, surprisingly, neither Optifree™ nor AQuify™ brand contact

lens care solutions, both of which contain active antimicrobial agents, had any significant effect on bioburden. Only the solution containing εPLL in the blister resulted in a statistically significant reduction in bacterial count ($p=0.00002$). The results are shown in Table 1.

[024] Table 1

Solution		Subject #							
		1	2	3	4	5	Ave	StDev	P value
PBS	Log CFU/Lens	2.3	2.8	2.4	3.0	2.8	2.7	0.27	
PBS + 500 ppm εPLL		1.1	0.7	0	0.3	0.8	0.6	0.39	0.00002
Optifree™		2.3	2.6	1.1	2.2	2.1	2.1	0.51	0.070
AQuify™		2.4	2.7	2.9	3.0	3.3	2.9	0.30	0.348
ClearCare™		0.5	2.5	2.3	2.8	.35	2.3	1.00	0.528

[025] These experiments indicate that handling is a significant source of microbial contamination of conventional hydrogel and silicone hydrogel contact lenses. εPLL is protective against environmentally-derived bacteria deposited on the lens by lens handling. The carryover of εPLL from a packaging solution significantly reduced bioburden delivered by handling.

[026] **Example 2: Lens handling assay - contamination of contact lenses from pathogens common in microbial keratitis**

[027] The bacterial adherence onto the surface of comfilcon A lenses removed from autoclaved blister packages containing a packaging solution of PBS with or without εPLL (10, 25, 100, or 500 ppm) was evaluated using a modification of methods described by Nomachi et al., *Eye & Contact Lens* (2013) 39:234-238. Briefly, the bacterial adherence onto the surface of comfilcon A contact lenses was evaluated using stock solutions of *Pseudomona aeruginosa* (PA) and *Staphylococcus aureus* (SA) prepared substantially as described in Example 3 below. Sterile surgical plastic gloves were put on both hands aseptically. After the seal of the comfilcon A package was opened, the thumb and index

finger of a hand gloved were dipped into the bacterial suspension (approximately 10^3 CFU/ml in PBS) and used to remove a lens from a package. Four lenses of each type of packaging solution were tested. Each lens was placed into a microcentrifuge tube with 1 mL PBS-T, sonicated for 1.5 minute and vortexed for 10 minutes at 1000 rpm. The entire volume of the extract was plated onto a culture dish with tryptic soy agar (TSA) and grown at 37°C for 2 days in an incubator.

[028] Table 2 below shows the average CFU/Lens (n=4) on contact lenses removed from the different packaging solutions.

[029] **Table 2**

Organism	0 ppm εPLL	10 ppm εPLL	25 ppm εPLL	100 ppm εPLL	500 ppm εPLL
PA	54	42	16	1	0
SA	43	37	35	21	7

[030] After removal of the contact lenses by finger and thumb contaminated with PA, as described above, the blister package and remaining packaging solution were left covered with the original blister foil at ambient temperature. After 16 hours, the entire volume of remaining packaging solution (~ 1mL) was plated onto a culture dish with TSA and left in an incubator at 37°C for 2 days to grow. The packaging solution without any added ePL had an average of 331 CFU/Lens. None of the ePL-containing packaging solutions exhibited microbial growth, i.e. all had 0 CFU/Lens.

[031] **Example 3: Preparation of bacterial suspensions**

[032] Cultures were prepared from growing a single colony of each of the bacterial species shown in Table 3 below in 50 mL trypticase soy broth (TSB) overnight at 37 °C on a rotary shaker. 1 mL of each culture was centrifuged, and the bacterial pellet resuspended in 1.0 mL of the diluent shown in Table 3. For each bacterial species, a suspension of approximately 10^8 CFU/mL was prepared by diluting the bacterial suspension to achieve the optical density indicated in Table 3. Each suspension is further

diluted for use in the handling assay described in Example 2 or the *in vitro* bioactivity assay described in Example 4.

[033] **Table 3**

Species	Strain	OD ₆₆₀	Media Diluent
PA	ATCC 99027	~0.1	0.01 % TSB in PBS-T
SA	ATCC 13880	~0.3	10.0 % TSB in PBS-T

[034] **Example 4: *In Vitro* Bioactivity Assay**

[035] A contact lens is removed from its packaging and rinsed in 2.5 ml sterile PBS for a few seconds (e.g. 4 seconds) to remove residual packaging solution. The rinsed lens is then transferred to an individual well of a 24-well plate containing 1.0 mL of 10⁴ CFU PA. The plate is incubated at 37°C with gentle shaking for 24 hours. The lens is removed from its well and transferred to a well of a 12-well plate containing 2.5 mL of sterile PBS. The plate is gently swirled for about 30 seconds. This step is repeated once for each lens.

[036] Each washed lens is placed in a microcentrifuge tube containing 1 mL of Dey-Engley (DE) neutralizing broth and adhered bacteria are removed by a combination of sonication for about 2 minutes and vortexing for about 10 minutes. Serial dilutions are made for each recovered cell suspension using DE neutralizing broth and suitable dilutions are plated onto TSA. Plates are incubated overnight at 37°C and CFUs are counted.

[037] The CFU for each plate is multiplied by the dilution factor (DF) as well as the plating dilution factor (PDF). The total CFUs recovered for a given sample are then converted to the log 10. To calculate the log kill of a contact lens packaged in a packaging solution comprising ePLL (i.e. the “test lens”), the log of CFU/lens of the test lens is subtracted from that of a control lens, which is identical to the test lens and packaged in an identical package and contact lens packaging solution except that the packaging solution lacks the ePLL. For example, if the mean log 10 value of an antimicrobial lens is 1.05 and the mean log 10 value of an otherwise identical control lens lacking the active antimicrobial agent is 5.52, the log kill is 5.52-1.05 = 4.47.

[038] Although 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.

[039] A number of publications and patents have been cited hereinabove. Each of the cited publications and patents are hereby incorporated by reference in their entireties.

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

1. A sealed contact lens package comprising a sterile, unworn contact lens and a contact lens packaging solution comprising epsilon polylysine (ϵ PLL), wherein the unworn contact lens exhibits reduced contamination from *Pseudomonas aeruginosa* (PA) introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in a substantially identical contact lens packaging solution without ϵ PLL.
2. A sealed contact lens package comprising a sterile, unworn contact lens and a contact lens packaging solution comprising epsilon polylysine (ϵ PLL), wherein the unworn contact lens exhibits reduced contamination from at least one microbe, wherein said reduced contamination is determined by a test where *Pseudomonas aeruginosa* (PA) introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in an identical contact lens packaging solution but without said ϵ PLL.
3. The package of any preceding or following embodiment/feature/aspect wherein, in the test, the unworn contact lens results in less than a two log kill of PA compared to the control contact lens when tested after 24 hours incubation with 10^4 CFU PA using an *in vitro* bioactivity assay.
4. The package of any preceding or following embodiment/feature/aspect, wherein, in the test, the unworn contact lens results in less than a one log kill of PA (but more than a zero

log kill) compared to the control contact lens when tested after 24 hours incubation with 10^4 CFU PA using an *in vitro* bioactivity assay.

5. The package of any preceding or following embodiment/feature/aspect, wherein the contact lens is a silicone hydrogel contact lens.
6. The package of any preceding or following embodiment/feature/aspect, wherein the contact lens is a non-ionic contact lens.
7. The package of any preceding or following embodiment/feature/aspect, wherein the contact lens is an ionic contact lens.
8. The package of any preceding or following embodiment/feature/aspect, wherein the contact lens is a daily disposable contact lens.
9. The package of any preceding or following embodiment/feature/aspect, wherein the contact lens is a daily wear contact lens.
10. The package of any preceding or following embodiment/feature/aspect, wherein the packaging solution comprises between 5 ppm and 500 ppm ϵ PLL.
11. The package of any preceding or following embodiment/feature/aspect, wherein the packaging solution comprises between 5 ppm and 50 ppm ϵ PLL.
12. The package of any preceding or following embodiment/feature/aspect, wherein the contact lens package further comprises (a) a plastic base member comprising i) a cavity which retains the unworn contact lens and the contact lens packaging solution, and ii) a flange region extending outwardly around the cavity; and (b) a removable foil attached to the flange region.
13. The package of any preceding or following embodiment/feature/aspect, wherein the contact lens package further comprises (a) a plastic base member comprising a cavity which retains the unworn contact lens and the contact lens packaging solution; and (b) a resealable cover that forms a liquid-tight seal with the plastic base member.
14. The package of any preceding or following embodiment/feature/aspect, wherein the plastic base member comprises a plurality of threads for engagement with a compatible set of threads on the resealable cover.
15. The package of any preceding or following embodiment/feature/aspect, wherein the at least one microbe is *Pseudomonas aeruginosa*.
16. The package of any preceding or following embodiment/feature/aspect, wherein the at least one microbe is *Staphylococcus aureus*.

17. The package of any preceding or following embodiment/feature/aspect, wherein the at least one microbe is a microbe found in microbial keratitis.

18. A method of manufacturing the sealed contact lens package, said method comprising placing an unworn contact lens and a contact lens packaging solution comprising ePLL in a receptacle configured to receive a contact lens and sealing the receptacle with a cover to provide a sealed contact lens package, wherein the unworn contact lens exhibits reduced contamination from *Pseudomonas aeruginosa* (PA) introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in a substantially identical contact lens packaging solution without ePLL, and wherein the unworn contact lens results in less than a two log kill of PA compared to the control contact lens when tested after 24 hours incubation with 10^4 CFU PA using an *in vitro* bioactivity assay.

19. A method of manufacturing the sealed contact lens package, said method comprising placing an unworn contact lens and a contact lens packaging solution comprising ePLL in a receptacle configured to receive a contact lens and sealing the receptacle with a cover to provide a sealed contact lens package, wherein the unworn contact lens exhibits reduced contamination from at least one microbe, wherein said reduced contamination is determined by a test where *Pseudomonas aeruginosa* (PA) introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in an identical contact lens packaging solution but without said ePLL, and wherein the unworn contact lens results in less than a two log kill of PA compared to the control contact lens when tested after 24 hours incubation with 10^4 CFU PA using an *in vitro* bioactivity assay.

20. The method of any preceding or following embodiment/feature/aspect, wherein the contact lens package is any one embodiment described above (e.g., 1 through 17.)

21. The method of any preceding or following embodiment/feature/aspect further comprising sterilizing the unworn contact lens by autoclaving the sealed contact lens package.

22. A method of manufacturing the sealed contact lens package, said method comprising placing an unworn contact lens and a contact lens packaging solution comprising ePLL in a receptacle configured to receive a contact lens and sealing the receptacle with a cover to provide a sealed contact lens package, wherein the unworn contact lens exhibits reduced

contamination from *Pseudomonas aeruginosa* (PA) introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in a substantially identical contact lens packaging solution without ePLL, and wherein the contact lens package comprises a resealable cover.

23. A method of manufacturing the sealed contact lens package, said method comprising placing an unworn contact lens and a contact lens packaging solution comprising ePLL in a receptacle configured to receive a contact lens and sealing the receptacle with a cover to provide a sealed contact lens package, wherein the unworn contact lens exhibits reduced contamination from at least one microbe, wherein said reduced contamination is determined by a test where *Pseudomonas aeruginosa* (PA) introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in an identical contact lens packaging solution but without said ePLL, and wherein the contact lens package comprises a resealable cover.

24. The method of any preceding or following embodiment/feature/aspect, wherein the contact lens package is any one of 1 through 17.

25. The method of any preceding or following embodiment/feature/aspect, further comprising sterilizing the unworn contact lens by autoclaving the sealed contact lens package.

[041] The present invention can include any combination of these various features or embodiments above and/or below as set forth in sentences and/or paragraphs. Any combination of disclosed features herein is considered part of the present invention and no limitation is intended with respect to combinable features.

[042] When an amount, concentration, or other value or parameter is given as either a range, preferred range, or a list of upper preferable values and lower preferable values, this is to be understood as specifically disclosing all ranges formed from any pair of any upper range limit or preferred value and any lower range limit or preferred value, regardless of whether ranges are separately disclosed. Where a range of numerical values is recited herein, unless otherwise stated, the range is intended to include the endpoints thereof, and all integers and fractions within the range. It is not intended that the scope of the invention be limited to the specific values recited when defining a range.

[043] 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.

CLAIMS:

1. An autoclaved sealed, contact lens package comprising a sterile, unworn non-ionic contact lens and a contact lens packaging solution comprising between 5 ppm and 250 ppm epsilon polylysine (ϵ PLL), wherein the unworn contact lens exhibits reduced contamination from at least *Pseudomonas aeruginosa* (PA) due to the presence of the ϵ PLL in the packaging solution, wherein said reduced contamination is determined by a test where PA introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in an identical contact lens packaging solution but without said ϵ PLL, and wherein the unworn contact lens results in less than a two log kill of PA compared to the control contact lens when tested after 24 hours incubation with 10^4 CFU PA using an *in vitro* bioactivity assay.
2. The package of claim 1, wherein the contact lens is a silicone hydrogel contact lens.
3. The package of claim 1 or claim 2, wherein the contact lens is a convention hydrogel contact lens formed from the polymerization of 2-hydroxyethyl methacrylate (HEMA) and/or vinyl alcohol optionally in combination with other monomers.
4. The package of any one of claims 1 to 3, wherein the contact lens is a daily disposable contact lens.
5. The package of any one of claims 1 to 4, wherein the sealed contact lens package comprises a plastic base member that comprises a cavity and a flange region extending outwardly around the cavity, and a removable foil attached to the flange region.

6. The package of any one of claims 1 to 5, comprising:
 - a) a plastic base member comprising a cavity which retains the sterile, unworn, non-ionic contact lens and the contact lens packaging solution comprising between 5 ppm and 250 ppm epsilon polylysine (ϵ PLL); and
 - b) a resealable cover that forms a liquid-tight seal with the plastic base member.
7. The package of claim 6, wherein the plastic base member comprises a plurality of threads for engagement with a compatible set of threads on the resealable cover.
8. The package of any one of claims 1 to 7, wherein the packaging solution comprises between 10 ppm and 150 ppm ϵ PLL.
9. The package of any one of claims 1 to 8, wherein the unworn contact lens exhibits reduced contamination from at least *Staphylococcus aureus* (SA) due to the presence of the ϵ PLL in the packaging solution, wherein said reduced contamination is determined by a test where PA introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in an identical contact lens packaging solution but without said ϵ PLL.
10. The package of any one of claims 1 to 9, wherein the unworn contact lens exhibits reduced contamination from at least one microbe is a microbe found in microbial keratitis due to the presence of the ϵ PLL in the packaging solution, wherein said reduced contamination is determined by a test where PA introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in an identical contact lens packaging solution but without said ϵ PLL.

11. A method of manufacturing a sealed contact lens package, said method comprising:
placing an unworn, non-ionic contact lens and a contact lens packaging solution comprising between 5 ppm and 250 ppm ϵ PLL in a receptacle configured to receive a contact lens;
sealing the receptacle with a cover to provide a sealed contact lens package; and
sterilizing the unworn contact lens by autoclaving the sealed contact lens package;
wherein the unworn contact lens exhibits reduced contamination from at least *Pseudomonas aeruginosa* (PA) due to the presence of the ϵ PLL in the packaging solution, wherein said reduced contamination is determined by a test where PA introduced to the lens during removal from the contact lens packaging solution compared to a control contact lens packaged in an identical contact lens packaging solution but without said ϵ PLL, and wherein the unworn contact lens results in less than two log kill of PA compared to the control contact lens when tested after 24 hours incubation with 10^4 CFU PA using an *in vitro* bioactivity assay.
12. The method of claim 11, wherein the contact lens package comprises a resealable cover.
13. The method of claim 12, for manufacturing the sealed contact lens package as defined in claim 6 or claim 7.
14. The method of claim 11, for manufacturing the sealed contact lens package as defined in any one of claims 2 to 4.
15. The method of any one of claims 11 to 14, wherein the packaging solution comprises between 10 ppm and 150 ppm ϵ PLL.