

Developments in lens care solutions

Nick Atkins describes the evolution of current contact lens care solutions, explains their mode of action, and describes where incompatibility may affect performance

CET Module C3113 (two contact lens points)

IT IS NOW 11 years since the introduction of multipurpose contact lens solutions in the UK. Since the historic launch of the first UK multipurpose solutions – Complete and ReNu – in the summer of 1994 and the switch from Medicine Control Agency to Medical Devices Agency control, with the introduction of CE marking from January 1 1995, there has been a flood of lens care solution introductions. AOSep is another solution that benefited from the change in regulatory control from 1995 and for the next 11 years there have been two basic types of ‘simpler’ systems dominating in varying proportions, the one-step hydrogen peroxide and the multipurpose solutions. The relative pros and cons of these products are shown in Table 1.

While during the mid-late 1990s the principal debate as to which was the best solution focused on MPS versus peroxide, there was also the parallel discussion as to which product was best within these two categories. In the peroxide category, was one-step as efficacious as two-step and in the MPS sector was (is) polyquarternium-1 (polyquad) better than polyhexinide? Increasingly and particularly as we entered this century the debate became more centred on the MPS category with the numerous polyhexinide formulations vs polyquad still the only protagonists. Polyhexinide is used most extensively in a variety of different companies’ formulations,

with Polyquad only available in Alcon Laboratories products such as Optifree Express. Table 2 shows examples of the basic formulation of a sample of these solutions.

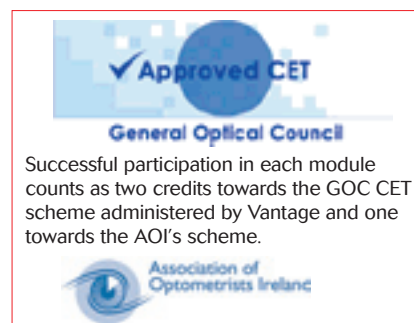
During this period practitioners have almost performed a complete turnaround in their prescribing habits, from a market dominated by one- and two-step hydrogen peroxide systems. According to the annual review of UK practitioner prescribing trends by Eurolens Research,¹ 91 per cent of care products recommended by practitioners in the 2005 survey period were multipurpose solutions.

With there being so many apparently similar products and generally happy patients, it is perhaps understandable that many practitioners seem to have become blasé about lens care and pay little attention to apparently subtle formulation differences. Consequently there seems to be a trend of thinking that all MPSs are ‘pretty much the same’.

THE ‘IDEAL’ SOLUTION

All the contact lens care products ever developed and commercialised have been trying to get closer the ‘Holy Grail’ of contact lens care. The ideal solution can be said to require the following key features:

- ◆ Kills all ocular pathogens
- ◆ Is non-toxic to the ocular surface



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- ◆ Simple to use
- ◆ Effectively removes deposits
- ◆ Affordable.

While other benefits may be desirable, particularly as we get closer to perfection, these are the core attributes required.

Over the past seven years, there have been many reformulations and new claims, of advanced cleaning and enhanced comfort. However, until 2004 the basic chemicals involved in the preservation and disinfection process had remained unchanged.

With silicone hydrogel lenses offering patients improved ocular health, prolonged comfort with the elimination of hypoxia and many practitioners reluctant to prescribe patients a continuous wear modality, it is reasonable to assume that the future for many wearers is to upgrade their hydrogel lenses and continue with daily wear and lens care. It should therefore be remembered that most solutions in common use today were developed before the advent of silicone hydrogel materials and so seamless compatibility between lens surface and care system is perhaps a naïve expectation. The first two silicone hydrogel lenses PureVision and Focus Night & Day were also developed with the prime objective of being worn continuously for 30 days and nights. When practitioners decided that they wanted to prescribe them for daily use, there was little data available as to either the short- or long-term implications for the daily soaking of the balafilcon A and lotrafilcon A materials in the numerous different solutions available.

This article is designed to bring practitioners up to speed with some of the latest developments in lens care solutions, our increasing understanding of their interaction with contact lens materials and ultimately to establish the importance of a considered approach to solution selection.

TABLE 1. MPS versus H₂O₂

Multipurpose solutions	Hydrogen peroxide systems
Advantages Selective antimicrobial action Continuous disinfection activity Simple to use Convenient single bottle	Advantages Potent, non-specific, rapid disinfection Preservative-free following neutralisation
Disadvantages Corneal staining with some lens/Px combinations Relatively poor disinfection efficacy against fungi and <i>Acanthamoeba</i>	Disadvantages Highly toxic without neutralisation Relatively impotent for long-term storage Complex, particularly in 2-step format

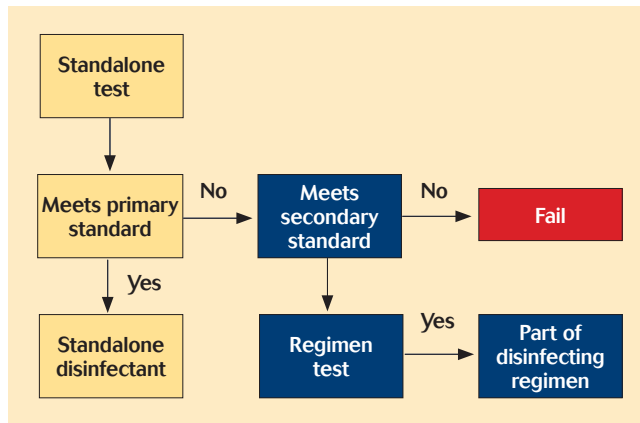


FIGURE 1. ISO standards ISO/DIS 14729. Flow chart indicating the process in obtaining ISO standard status

ARE MPS CREATED EQUAL?

For those that read the research and understand the delicate balance that exists between ingredients in a formulation and the interaction of that formulation with different lens materials and the deposits that can form on those different lenses, the answer to this question has always been a definite 'No'.

Disinfection

Disinfection is one of the primary objectives of a contact lens soaking solution and since 1995 has been covered by ISO standards, with a CE mark being placed on products meeting the standard in the European Union. With all commercialised solutions having achieved a CE mark, it is perhaps understandable how practitioners might assume them to be equal, but while an important safety control, the only standards to which solutions must adhere are those for disinfection. All other aspects of performance must simply be supported by clinical data in the product technical file.

Antimicrobial activity

ISO/DIS 14729 is the standard for the antimicrobial efficacy of lens care products and Figure 1 shows how a solution can meet the standard either as a stand-alone disinfectant or as part of a regimen where a rub and rinse is required. The standard requires the solutions to demonstrate the required log reduction against three bacteria and two fungi. The primary standard for stand-alone disinfection requires a 1 million organisms/ml challenge (6 log units) and for the organisms to be killed to the levels shown below:

Bacteria

- ◆ 99.9 per cent (3 log) reduction in stated soaking time
- ◆ *Staphylococcus aureus*
- ◆ *Pseudomonas aeruginosa*
- ◆ *Serratia marcescens*.

Fungi

- ◆ 90 per cent (1 log) reduction in stated soaking time
- ◆ *Candida albicans*
- ◆ *Fusarium solani*.

It is not the intention of this article to review the relative performance of lens care products' antimicrobial performance as all those for sale, as previously stated, meet the ISO standards to a greater or lesser extent and are able to carry the CE mark.

Anti-Acanthamoeba activity

It is interesting to observe that the apparent obsession with performance against *Acanthamoeba* seen in the 90s has become more balanced. This is in line with the low number of reported cases presenting with this debilitating infection source.² Equally interesting is that this also coincides with the almost complete use of solutions that some quarters of the profession chastised for their lack of *Acanthamoeba* activity.

In fact, multipurpose solutions do have an effect on *Acanthamoeba* counts whether by simple physical removal or some level of disinfection. Additionally, it seems highly likely their multifunctional approach, in that they do not necessitate nor inadvertently encourage the use of tap water in the regimen, plays an important part in this outcome.

There are currently no agreed test organisms or standards to which solutions must conform in their efficacy against *Acanthamoeba*. However, as a consequence of this fact, clinicians should take care in comparing the claimed performance against amoeba and it is this author's opinion that claims of anti-*Acanthamoeba* performance have no place on the product packaging. This advice was supported in a recent study that concluded that when used as recommended by their manufacturer, some MPSs are more effective than others at killing the representative strains of *Acanthamoeba*.³

Responsibly manufacturers are continuing funding research into the

performance of their products against *Acanthamoeba*, usually testing against trophozoites and cysts for the species *A polyphaga* and *A castellani*. The continued use of a cleaning step would seem to be the best protection against contamination by this organism. It has been shown that the complete mechanical removal of *A polyphaga* can be achieved using the recommended 60-second cycle of the Complete Rapidcare cleaning device.⁴

'No rub'

The recommendation that no cleaning was required was first seen with Alcon's Opti-1 solution for two-weekly replacement lenses. The first all-encompassing 'no rub' claim came from the same company's Optifree Express solution early this decade. It is important to understand that the development of 'no rub' claims is a reflection of a solution's disinfection efficacy, not its cleaning ability.

Subsequent to Alcon's lead, most MPS solutions have adopted this claim by demonstrating data supporting at least a 3 log unit and 1 log unit reduction in bacteria and fungi respectively, in the presence of organic soil (thus meeting ISO/DIS 14729). The most notable exception is the original ReNu MPS with its lowest concentration of polyhexanide (0.00005 per cent).

THE OLD 'NEW GENERATION'

Since 1995 there have been new formulations and reformulations, with the introduction of advanced cleaning and comfort enhancing agents to further improve product performance. During the 90s the debate as to the best solution focused on MPS versus peroxide and, within the MPS category simply considered polyhexanide versus polyquad.

Polyhexanide

Also known as polyhexymethylene biguinide (PHMB), polyaminopropyl biguinide (PAPB) and commercially as 'Dymed' in the original MPS, ReNu from Bausch & Lomb, polyhexinide is one of the first of the so-called 'new generation' preservatives.

Polyhexinide is a biguinide, belonging to the same pharmaceutical family as chlorhexidine. However, it differs in that it is a long-chain polymer (molecular weight of 1,300 compared to the 359 of chlorhexidine) with 6-8 active sites which bind to phospholipids in the cytoplasmic membrane, disrupting it, causing loss of the cell constituents and cell death.

Polyhexanide, as previously mentioned, has been widely used in the contact lens industry in varying concentrations from 0.00005 per cent (0.5 ppm) to 0.005 per cent (50 ppm) as shown in Table 2.

TABLE 2. Examples of multipurpose solutions formulations

Product	Manufacturer	Disinfectant	Concentration	Surfactant	Additional lubricant/conditioners
ReNu	B&L	PHMB	0.5 ppm	Poloxamine	None
Focus Aqua	CIBA Vision	PHMB	1.0 ppm	Pluronic F127	Dexpathenol
Complete Moisture Plus	AMO	PHMB	1.0 ppm	Poloxamer 237	HPMC 0.15% propylene glycol 0.5%
All in One	Sauflon	PHMB	5.0 ppm	Poloxamine	None
Opti-1	Alcon	Polyquad	11.0 ppm	None	None
Opti-Free Express	Alcon	Polyquad	11.0 ppm	Poloxamine	Aminomethylpropanol
		Aldox*	5.0 ppm		

*Myrisamidopropyl dimethylamine

Polyquad

Polquaternium-1 (a polymeric quaternary ammonium compound) to give it its chemical name, is the largest polymeric molecule used for contact lens disinfection and is found only in Alcon solutions. With a molecular weight of 5,000 it resists diffusion into the lens matrix, minimising the toxic hypersensitivity reactions found with the traditional smaller preservatives such as chlorhexidine and thiomersal. Polyquad's affinity for binding to methacrylic acid found in many modern contact lens materials was resolved early on by formulation changes.

Its relatively poor performance against fungus and *Acanthamoeba* was also addressed by its formulation with MAPD (myristamidopropyl dimethylamine), commercially known as Aldox, with the introduction of Optifree Express.⁵

UNDERSTANDING INCOMPATIBILITIES

A number of criteria must be considered when selecting a solution for an individual patient and the principal ones are:

- ◆ Detailed patient history
- ◆ Lens material to be/being worn
- ◆ Patient compliance potential.

It has long been known that even the modern polymeric preserved solutions can cause corneal staining.^{6,7} Staining and subjective comfort can vary depending



FIGURE 3. The Regard MPS range

on the formulation and concentration of polyhexanide⁸ and particularly with higher concentrations used in conjunction with high water, FDA Group II materials.^{9,10} Numerous studies comparing polyhexinide with both hydrogen peroxide and polyquaternium-based solutions, have shown higher levels of staining with polyhexinide.^{9,10,11}

More recently it has been found that both polyhexinide and polyquad-based MPSs used with both balafilcon A (PureVision) and lotrafilcon A (Focus Night & Day) will demonstrate a varying incidence and severity of staining^{12,13} and that identical concentrations of polyhexinide can behave differently, depending on solution formulation.^{14,15} In the Jones *et al*

study¹² 37 per cent of PureVision wearers using ReNu MultiPlus demonstrated a solution-based reaction with 11 subjects requiring discontinuation from the study.

Confusingly for practitioners the age-old maxim of 'if it ain't broke, don't fix it' seems not to apply with reports suggesting confirmation of the author's personal experience, that signs and symptoms of solution intolerance may occur with continued usage of a previously successful MPS when refitting from hydrogel to silicone hydrogel materials.¹⁶

THE ROLE OF LIPID

Although not completely understood, it would appear that lipids deposited on the surface of high water non-ionic hydrogel as well as low water ionic silicone hydrogel lenses are a factor in the increased corneal staining sometimes observed. The binding of polyhexinide to the lipid deposits on the silicone hydrogel lens surface increases their exposure to the epithelium by acting as a kind of drug delivery system.¹⁷ Interestingly, the staining is usually asymptomatic and appears as a ring over the peripheral cornea, limbal area and adjoining conjunctiva and is greatest in the inferior cornea.¹² This forms a so-called 'doughnut' pattern as shown in Figure 2.

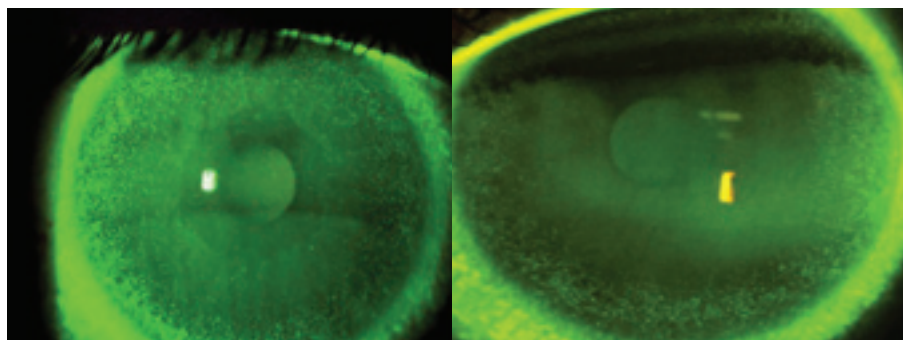


FIGURE 2. Doughnut staining pattern. Images courtesy of Lyndon Jones, CCLR



TABLE 3. Composition of Regard Multipurpose

Components	Action
NaClO ₂ H ₂ O ₂	Disinfection Stabilisation/re-activation of disinfection
Pluronic F-68 Hydroxypropylmethylcellulose	Cleaning/lubrication Lubrication

THE NEW 'NEW GENERATION'

Polyhexinaide and polyquad reigned supreme until 2004 when a couple of new entrants challenged the preservation and disinfection status quo. This year saw the introduction of solutions using sodium chlorite (Regard) and alexidine (ReNu MoistureLoc) as disinfectants.

SODIUM CHLORITE

A new MPS, Regard (Figure 3) was presented, via a poster, at the BCLA meeting in May 2003¹⁸ and is marketed through Advanced Eyecare Research. It came to the attention, interest and use of the author due to its claimed 'preservative free' method of disinfection. The key components of Regard can be seen in Table 3.

The chlorite/peroxide complex in Regard is an active anti-microbial agent and has been reported as safe and non-irritating to the corneal epithelium.¹⁸ The complex molecule is self-stabilised in the bottle or lens case and rapidly degrades into salt, water and oxygen in the ocular environment.

Sodium chlorite generates chlorine dioxide which is very effective in killing Gram +ve and Gram -ve bacteria, yeasts and fungi, subsequently breaking down into the components of natural tears:

- ◆ Salt
- ◆ Water
- ◆ Oxygen.

Sodium chlorite is activated by acidic cellular components and has been used safely for many years as a treatment for municipal drinking water. The chlorite/peroxide formulation is based on the synergistic microbial activities of both chemicals. Once the contact lenses are removed from the solution (which maintains stability) sodium chlorite breaks down into sodium chloride and oxygen.¹⁹

ALEXIDINE

In late 2004 Bausch & Lomb launched its replacement for ReNu MultiPlus, ReNu MoistureLoc (Figure 4) and while marketed on the benefits of its moisture retaining properties, many practitioners will have missed the most important aspect (in this author's opinion) of the new solution; the introduction of a brand

TABLE 4. Composition of ReNu MoistureLoc

Components	Action
Alexidine	Disinfection
Hydranate	Protein sequestration
Polyquarternium-10	Deposit inhibitor
Poloxamine	Cleaning/lubrication
Poloxamer 407	Lubrication

new disinfectant to the contact lens sector – alexidine. The key components of ReNu MoistureLoc can be seen in Table 4.

Alexidine has a track record in the mouthwash industry in the same way as polyhexanide was 'borrowed' from its use in swimming pools and is also from the same biguinide family of disinfectants. However, there are differences between alexidine and polyhexanide. Alexidine, a bis-biguinide, is a smaller molecule that contains two active sites and is used in a concentration of 0.0045 per cent in the contact lens solution. Similar to polyhexanide, these biguinide groups interact with and disrupt the acidic phospholipid groups in a micro-organism's cytoplasmic membrane, the membrane disintegrates and the cell components are released.

The ReNu MoistureLoc formulation has demonstrated its efficacy against the ISO test panel²⁰ and trophozoites and cysts of *Acanthamoeba* strains *A Castellani* and *A Polyphaga*.⁵ It also demonstrated good compatibility with the eye, even with silicone hydrogel lenses.²⁰



FIGURE 4. ReNu MoistureLoc MPS

DISCUSSION

As some manufacturers turn their attention to other attributes such as improving the lens comfort and hydration characteristics, it is important for practitioners to remember the fundamental function of lens care before being bedazzled by slick marketing into basing their solution recommendation on the 'nice to have' attributes rather than the 'need to have' performance.

Unfortunately, many practitioners, perhaps due to having no background in chemistry or microbiology, seem to rely more on the manufacturers for information in this area than in any other area of CL practice; perhaps then this helps explain the apparent low priority placed on considering selection of the most appropriate solution. Perhaps with this reliance on company data, practitioners are also somewhat sceptical as to how commercially biased this information is. 'Surely the claimed superiority in performance difference can't be so great, when a quick check of the bottle ingredients suggests such similarity?' So maybe the claims and counterclaims of the companies have inadvertently made practitioners more sceptical and less interested, rather than encouraging them to take more interest and place more importance on understanding what is in the products they recommend their patients put in their eyes?

CONCLUSION

A delicate balance exists between the contact lens and its care system and the health of the ocular surface in contact lens wear. Many practitioners need to reconsider the priority they place on lens care selection. Any believing that all solutions are the same or similar are advised to take another look at the new products on the market and ensure that they are familiar with the differences in their mode of action and formulations and consequently their interaction with different lens materials. The correct selection of lens care product has the potential to significantly improve the comfort and wearing times of many patients. Along with the appropriate selection of contact lens material and modality, this will have an important role to play in the long-term success of individual contact lens patients.

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MULTIPLE-CHOICE QUESTIONS

- 1 Which of the following statements is false?**
- A Some MPSs are more effective than others at killing representative strains of *Acanthamoeba*
- B Polyhexinide and polyquad based MPSs used with silicone hydrogels will demonstrate a varying incidence and severity of staining
- C The binding of polyhexinide to the lipid deposits on the silicone hydrogel lens surface increases their exposure to the epithelium by acting as a kind of drug delivery system
- D Numerous studies comparing polyquarternium with both hydrogen peroxide and polyhexinide based solutions, have shown higher levels of staining with polyquarternium
- 2 Polyquarternium-1 is also known as:**
- A PHMB
- B Polyquad
- C Dymed
- D PAPB
- 3 Regard contains:**
- A Hydrogen peroxide
- B Alexidine
- C MAPD
- D Chlorhexidine
- 4 Which statement is true about alexidine?**
- A It is borrowed technology from disinfecting swimming pools
- B It has 6-8 active binding sites
- C It has been shown to cause significant staining with silicone hydrogels
- D It demonstrates disinfection efficacy against *Acanthamoeba*
- 5 Before January 1, 1995, lens care products were regulated by:**
- A British Standards
- B Medical Device Agency
- C Medicines Control Agency
- D Was unregulated
- 6 Which of the following is not a core attribute required for a contact lens solution?**
- A Toxic to ocular pathogens
- B Simple to use
- C Removes deposits
- D Enhances lens comfort
- 7 Which of these solutions is 'preservative free'?**
- A Regard
- B Optifree Express
- C Complete
- D None of the above
- 8 Polyhexanide has been commercially available in the following concentrations:**
- A 50-500 ppm
- B 0.00005%-0.0005%
- C 5-50ppm
- D 0.0005%-0.005%
- 9 Which preservative has a molecular weight of 5,000?**
- A Alexadine
- B Polyhexanide
- C Polyquarternium-1
- D Sodium chlorite
- 10 Polyhexanide is not found as a preservative in:**
- A ReNu MoistureLoc
- B Focus Aqua
- C All In One
- D None of the above
- 11 Lens care products in the UK need meet which of the following standards:**
- A EU standards for CE marking
- B FDA
- C ISO/DIS 14729
- D ISO 9001
- 12 Acanthamoeba keratitis appears to be in decline in the UK:**
- A Because MPSs reduce the need for tap water use in the regimen
- B Despite MPSs displaying varying efficacy against disinfection of *Acanthamoeba*
- C Because *Acanthamoeba* are removed by the rub and rinsing step
- D All of the above

The deadline for response is March 2

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