



This is part 2 of two CET articles looking at the state-of-play in the lens care field and looks at the latest product developments, solution ingredients and formulations. Part 1 has already set the scene by looking at the current thinking and likely improvements that could be made to the regulation and testing of contact lens solutions.

Are you still supplying your solution starter kit based on what is in the cupboard and nearest to hand at the time? Hopefully not, but this article is intended to help clinicians review what they use against the latest products available, in order to formulate a strategy for the solutions they stock and then consider which is most appropriate for each of the individual patient and lens combinations in the chair.

It is now more than 16 years since the introduction of multipurpose contact lens solutions in the UK with the historic launch of Complete and ReNu – in the summer of 1994. The switch from Medicine Control Agency to Medical Devices Agency (now the MHRA) control, with the introduction of CE marking from January 1 1995, resulted in a flood of lens care solution introductions. The UK's first one-step hydrogen peroxide, AOSep, was one solution that benefited from the change in regulatory control and for the next 10 years or so there were two basic types of 'simpler' systems dominating in varying proportions – the one-step peroxide and the multipurpose solutions.

Multipurpose vs hydrogen peroxide

During the mid to late 1990s the principal debate as to which was the best solution focused on MPS versus peroxide, but 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 multipurpose solution (MPS) sector was polyquaternium-1 (polyquad) better than polyhexinide? Increasingly, particularly as we entered this century, the debate became more centred on the MPS category with the numerous polyhexinide formulations versus polyquad still the only protagonists. Polyhexinide is used most extensively in a variety of different companies' formulations; polyquad, until a few months ago, was only available in Alcon Laboratories' products such as Optifree Express and Optifree Replenish. Table 1 shows examples of the basic formulation of a historic sample of these solutions.

Contact lens care

Part 2 - Latest developments

Nick Atkins concludes his series looking at care systems with a revision of the latest developments in lens care. **Module C15770**, one CL point for CLOs, one general CET point for optometrists and dispensing opticians

TABLE 1

Examples of single disinfectant multipurpose solution formulations past and present

Product	Manufacturer	Disinfectant	Conc'n (ppm)	Surfactant	Additional lubricant/conditioners
ReNu	B+L	PHMB	0.5	Poloxamine	None
Focus Aqua	CIBA Vision	PHMB	1.0	Pluronic F127	Dexpathenol
Complete Easy Rub	AMO	PHMB	1.0	Poloxamer 237	None
All in One	Sauflon	PHMB	5.0	Poloxamine	None
Opti-1	Alcon	Polyquad	11.0	None	None

By the middle of the last decade, practitioners had 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 in 2005,¹ the use of multipurpose solutions peaked at 91 per cent of care products recommended by practitioners. There was a slight dip in this figure subsequently, with multipurpose solutions recovering to 89 per cent of care products recommended by practitioners in the 2010 survey.² It is likely that events such as the product withdrawals due to infection outbreaks as well as concerns about staining levels with certain lens/solution combinations might have led some practitioners to increase their use of peroxide-based systems. It is important to remember, however, that no system is a panacea and that each case needs to be judged on its merits. Certainly MPSs would not have come to dominate the market if they did not have significant advantages for both patient and practitioner.

While peroxide is effective against a large number of strains of *Acanthamoeba* trophozoites and cysts, it requires a long soaking time which many wearers will only find convenient if left in 3 per cent peroxide overnight. With no major manufacturer offering a two-step peroxide and a minimum four-hour

neutralisation period with the one-step products, clearly peroxide is not the definitive answer. Also, as mentioned in Part 1 of this series, reports of *Acanthamoeba* keratitis in the UK have been in decline during the same period of MPS growth and market dominance, which is unlikely to be coincidental.

All solutions are NOT the same

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 the proliferation of silicone hydrogel lenses offering patients improved ocular health and prolonged comfort 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 and care system is perhaps a naive expectation.

Despite many solutions appearing to be similar, those that read the research will understand that no one solution is the same as another. A delicate balance



exists between the ingredients in a solution formulation and the interaction of that formulation with different lens materials and the deposits that can form on those different lenses.

'New generation' preservatives

Early this decade the debate as to the best solution focused on the MPS category and whether polyhexanide or polyquad was superior as a disinfectant. They reigned supreme until 2004 when two new preservation systems, sodium chlorite and alexidine, challenged the preservation and disinfection status quo widening the debate.

Polyhexanide

Also known as polyhexymethylene biguinide (PHMB), polyaminopropyl biguinide (PAPB) and commercially as Dymed in the original MPS, ReNu from Bausch+Lomb, polyhexinide was 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 long chain polymer (molecular weight of 1,300 compared to the 359 of chlorhexidine) with 6-8 active sites. These bind to phospholipids in the cytoplasmic membrane disrupting it, causing loss of the cell constituents and cell death. Polyhexanide has been widely used in varying concentrations from 0.00005 per cent to 0.0005 per cent as shown in Table 1.

Polyquad

A polymeric quarternary ammonium compound, Polquaternium-1, to give it its chemical name, is the largest polymeric molecule used for contact

TABLE 2

Composition of Regard multipurpose solution

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

lens disinfection and until last autumn it could only be found 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. Originally used in isolation in Optifree, its relatively poor performance against fungus and *Acanthamoeba* was addressed by its formulation with MAPD (myristamidopropyl dimethylamine), commercially known as Aldox, with the introduction of Optifree Express.³

Sodium chlorite

Sodium chlorite was first seen in a MPS when Regard (Figure 1) was presented, via a poster at the BCLA meeting in May 2003⁴ and has subsequently been employed by Sauflon in its Synergy product. Regard 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 2.

Sodium chlorite is activated by acidic cellular components and has been used



Figure 1 Sodium chlorite was first seen in Regard MPS

safely for many years as a treatment for municipal drinking water. Sodium chlorite generates chlorine dioxide which is very effective in killing Gram+ and Gram- bacteria, yeasts and fungi, subsequently breaking down into the components of natural tears – salt, water and oxygen.

The chlorite/peroxide complex in Regard is an active anti-microbial agent and is safe and non-irritating to the corneal epithelium.⁴ The formulation is based on the synergistic microbial activities of both chemicals and once the contact lenses are removed from the solution (which maintains stability) sodium chlorite breaks down into sodium chloride and oxygen.⁵

Alexidine

In late 2004 Bausch+Lomb (B+L) launched ReNu with MoistureLoc. It was marketed on the benefits of its moisture-retaining properties, but many practitioners will have missed the most important aspect of the solution – the introduction of a brand new disinfectant to the contact lens sector, namely alexidine.

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. Similar to polyhexanide, these biguinide groups interact with and disrupt the acidic phospholipid groups in a micro-organism cytoplasmic membrane; the membrane disintegrates and the cell components are released. Alexidine can now be found in Complete RevitaLens and so it is important to realise that alexidine was never implicated in the global withdrawal of ReNu with MoistureLoc. The outbreak of *Fusarium* keratitis, mainly in Asia Pacific, was largely due to non-compliance and the protection

TABLE 3

Examples of dual disinfectant multipurpose solution formulations

Product	Manufacturer	Disinfectants	Conc'n (ppm)	Surfactant	Additional lubricant/conditioners
Biotrue	Bausch+Lomb	PHMB Polyquad	1.3 1.0	Poloxamine (Tetronic 1107)	Hyaluronic Acid
Complete RevitaLens	Abbot Medical Optics	Alexidine Polyquad	1.6 3.0	Poloxamine (Tetronic 904)	None
Opti-Free Express	Alcon	Polyquad Aldox*	11.0 5.0	Poloxamine (Tetronic 1304)	Aminomethyl-propanol
Opti-Free Replenish	Alcon	Polyquad Aldox*	11.0 5.0	Poloxamine (Tetronic 1304)	nonanoyl ethylene-diamine-triacetic acid (Tearglyde)

*Myristamidopropyl dimethylamine



TABLE 4

Composition of Biotrue and Complete RevitaLens multipurpose solutions

	Biotrue	Complete RevitaLens
Preservatives	PHMB 0.00013% 0.0001% polyquaternium-1	0.00016% alexidine 0.0003% polyquaternium-1
Buffer	Boric acid; sodium borate	Sodium borate; boric acid
Chelating agent	EDTA (%)	0.05% EDTA
Surfactant/ wetting agents	Poloxamine (Tetronic 1107)	Tetronic 904
Other	Hyaluron (hyaluronic acid - glycosaminoglycan) sulfobetaine (zwitterionic detergent)	Trisodium citrate



Figure 2 AMO's Complete RevitaLens and Biotrue by B+L

afforded to the fungi by the synthetic 'biofilm' left in lens cases, largely due to a combination of evaporation and the topping up of the solution in the case.

Dual disinfectants

Those as 'experienced' as the author will remember the combined use of chlorhexidine and thimerosal as dual disinfectants, in varying concentrations, in early chemical disinfecting solutions such as Hydrosoak from Contactasol. Chlorhexidine is more effective but has poor fungicidal capacity. Thimerosal is slower acting but is known to be a more effective antifungal agent. It is interesting to note that following the global withdrawal of one of their brands, both Abbot Medical

TABLE 5

MPS containing hyaluronic acid

Solution Name	Disinfectant	Company
Biotrue	PHMB/Polyquad	Bausch+Lomb
Eyeeye Imaxx (All in One)	PHMB	No 7
Unica Sensitive	PHMB	Avizor

Optics (AMO) and B+L have recently introduced solutions using a dual disinfection approach similar to Alcon with its Optifree products. Table 3 shows examples of the dual disinfecting solutions currently available.

AMO with Complete RevitaLens and B+L with Biotrue (Figure 2)

take different approaches to their formulations. A more detailed review of their ingredients is shown in Table 4.

Other additives

Over the past decade there has been a great deal of research and development into creating a contact lens solution that can enhance lens comfort and wearing time. The challenge is that adding additional and arguably non-essential ingredients complicates the formulation and inevitably results in compromises with other aspects of the solution's performance. To date, manufacturers have used a variety of surfactant and wetting agents, such as hydroxypropylmethylcellulose (HPMC), polyvinyl alcohol (PVA) and polyvinyl povidone (PVP) commonly found in dry eye drops. The cellulose-based agents such as HPMC are polysaccharides and so a potential food source for microorganisms, which is why great care is taken in the formulation process. Recently a number of solutions have incorporated another polysaccharide used in dry eye preparations, namely hyaluronic acid (Table 5), in an attempt to improve the lens comfort enhancing effect during lens storage.

Hyaluronic acid (HA)

HA, also known as sodium hyaluronate or hyaluronan, is a naturally occurring linear structured polysaccharide that is found in the aqueous and vitreous humour and the synovial fluid of joints. It is a non-toxic, viscoelastic, biological polymer that has good water binding properties to reduce evaporation. It also mimics the natural tear film in becoming more elastic during the blink, increasing spreading and improving aqueous lubrication of the anterior ocular surface epithelial tissues. This is known as rheological or non-Newtonian behaviour. Importantly, and supporting its use in a contact lens solution, is the fact that

MULTIPLE-CHOICE QUESTIONS - take part at opticianonline.net

1 Polyquaternium-1 is also known as:

- A Dymed
- B PHMB
- C Polyquad
- D Polyhexinide

2 Regard contains:

- A Hydrogen peroxide
- B Alexidine
- C MAPD
- D Polyhexanide

3 Which of the following statements is true about alexidine?

- A It is borrowed technology from disinfecting swimming pools
- B It has been used before in ReNu MultiPlus
- C It demonstrates poor disinfection efficacy against *Fusarium*
- D It is a small molecule with two active binding sites

4 Which of these solutions is 'preservative-free'?

- A Optifree Replenish
- B Synergy
- C Complete RevitaLens
- D Biotrue

5 Polyhexanide has been commercially available in the following concentrations:

- A 50-500 ppm
- B 0.00005 per cent-0.0005 per cent
- C 5-50ppm
- D 0.0005 per cent-0.005 per cent

6 Which preservative has a molecular weight of 5,000?

- A Alexidine
- B Polyhexanide
- C Polyquad
- D Sodium chlorite

Successful participation in this module counts as one credit towards the GOC CET scheme administered by Vantage and one towards the Association of Optometrists Ireland's scheme. The deadline for responses is March 3 2011.





HA has been shown to increase tear break-up time when used in eye drops.⁶

Discussion

Contact lens solutions are quite complex formulations and arguably more complex from a formulation perspective than most drugs. The latter are generally formulated with only one objective, but contact lens solutions have to perform numerous functions and ultimately formulation is a balancing act derived from compromise.

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 contact lens practice; perhaps with this reliance on company data, practitioners are also somewhat sceptical as to how commercially biased this information is.

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. Anyone who believes 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. 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.

Ultimately it is the partnership between industry, government, practitioners and our patients, that will improve the balance between contact lens success and failure. The correct selection and use of lens care will continue to have significant impact on which group a patient falls into, for many years to come. ●

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● **Nick Atkins** is a contact lens optician and professional affairs/marketing consultant to the optical industry. He is also a co-director of Proven Track Record, the force behind Independents Day and co-director of in-practice sales and training company Positive Impact. Atkins is a past president of the British Contact Lens Association and a director on the board of the Association of British Dispensing Opticians



UV blocking and O₂

Q Does the inclusion of an ultraviolet filter affect the Dk of a soft or gas-permeable contact lens?

A **Richard Ward replies:** In considering the potential impact of the UV blocker on these two material groups, it will be easier to deal with each material type separately.

Firstly, in adding a compound such as UV filters or blockers, it is important to recognise what is required in obtaining a good acceptable lens material. The development of such compounds is all about balancing the final material's properties through optimised formulations. So for the material to be clinically acceptable, its overall performance needs to show a balance between its bulk properties (modulus, strength, water content, transmission/RI and Dk) and its surface characteristics, such as wettability.

When considering the effects of UV on the different materials, I will look at the standard (non-silicone) hydrogels first. It is widely recognised that the oxygen permeability (Dk) of the material is entirely down to the material's water content and, as such,

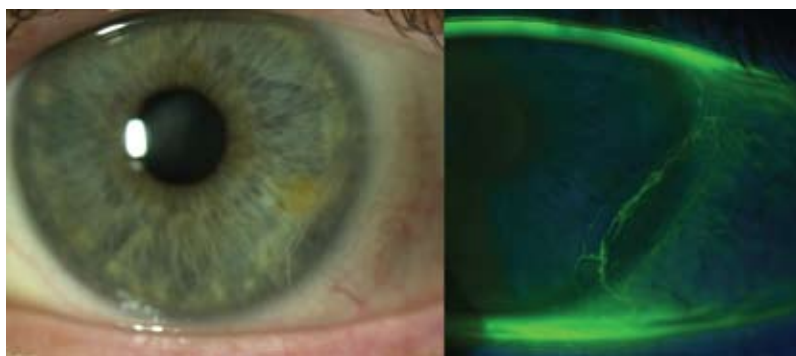
in adding the UV filter the chemist has to consider the impact of the filter compound on the water content.

The most commonly used UV-blocking compounds in standard hydrogels are known to be hydrophobic. Consequently, the inclusion of these within the polymer matrix will have a natural tendency to reduce the water content of the resulting material. So if the material's formulation is not readjusted to maintain its final water content, then yes the oxygen permeability of the material will be impacted. However, it is quite straightforward to re-adjust the formulation in such a way as to ensure the water content levels remain at the desired amount.

With gas-permeable contact lenses, given that the oxygen permeability is not related to water content but a function of the silicon or fluorinated content of the formulations, the presence of another hydrophobic compound within its formulation may not be quite as dramatic. Again, the material scientist will be able to incorporate the UV filter compound within the material formulation and, through readjustment of the other main components, maintain the final material's oxygen permeability.

So, in summary, yes the inclusion of UV filters can have an impact on the material's oxygen permeability characteristics, but it is possible to minimise these effects by slight material formulation adjustments, especially as these filter compounds are usually present in relatively low formulation concentrations.

● **Richard Ward** is director technology transfer at CooperVision UK



WHAT'S THIS?

Answer to What's this? (07.01.11):

The image shows threads trapped under a soft lens. On removal, the imprint of the threads is seen more easily with fluorescein. The patient experienced no discomfort. The images are courtesy of Andrew Gasson