

Effective Care Solution for Healthier Eyes

Disinfection / cleaning system for soft contact lenses

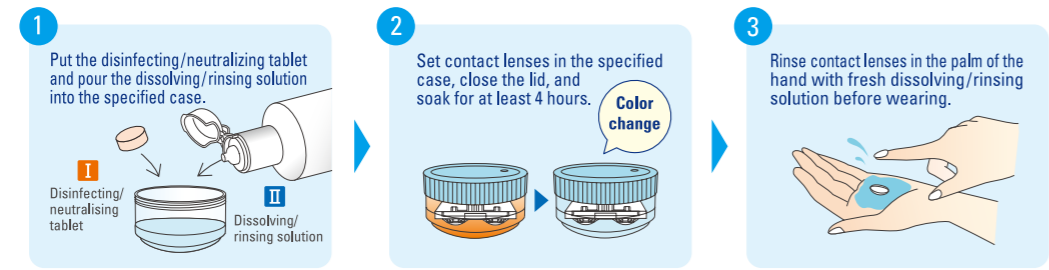
cleadew

ADVANCED CARE SYSTEM

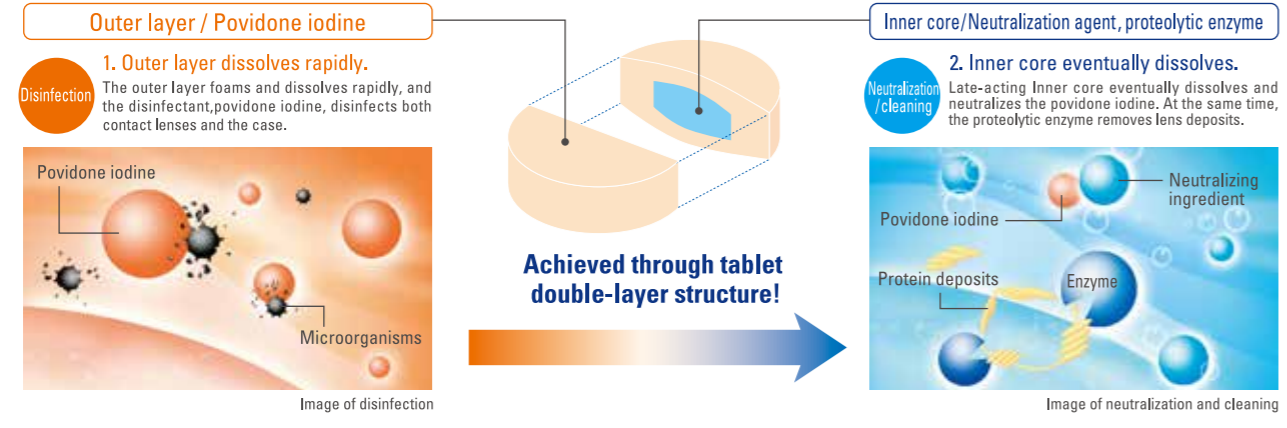
Product Information

Usage

- Before handling contact lenses, be sure to wash hands thoroughly with soap.
- For safe use of contact lenses, rub and rinse lenses with commercially available storing/rinsing solution for soft contact lenses or saline solution before disinfection.



cleadew automatically promotes disinfection, neutralization, and cleaning.



Summary of product characteristics

<b>Indications</b>	Disinfection for soft contact lenses (Group I to Group IV)	
<b>Dosage and administration</b>	<ol style="list-style-type: none"> <li>1. Pour the dissolving / rinsing solution up to the line marked on the lens case (8 mL), and then put a disinfection / neutralization tablet into the case.</li> <li>2. Place contact lenses in the case, and close the lid.</li> <li>3. After soaking the lenses for at least 4 hours, take the lenses out of the case and rinse them thoroughly with the dissolving / rinsing solution.</li> </ol>	
<b>Ingredients</b>	cleadew <b>I</b> (Disinfecting / neutralising tablet) (Active ingredient) Outer layer: Povidone iodine 4.0 mg / tablet Inner core: Ascorbic acid 2.0 mg / tablet (Ingredients) Foaming agent, excipient, lubricant, cleaning agent, coating agent	cleadew <b>II</b> (Dissolving / rinsing solution) Buffering agent, stabilizer, tonicity adjusting agent, pH adjusting agent (Display specified ingredients) Boric acid, Edetate



# Seeking safer, more guaranteed disinfection

Evolving disinfecting systems for soft contact lenses to minimize the risk of “eye infection”

cleadew



2013  
Povidone-iodine based disinfectant

Compared with conventional disinfectants

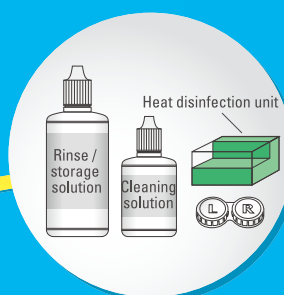
- **Improvement in disinfection efficacy**  
Effective against acanthamoeba, biofilm
- **Improvement in cleaning effect**  
Clean using proteolytic enzyme each time
- **Consideration of effects on corneal epithelial cells**

## Features of cleadew

- Highly safe and effective povidone iodine is used as disinfectant which enables complete disinfection of lenses.
- cleadew is the only disinfectant for soft contact lenses containing proteolytic enzyme which removes protein deposits in every application and keeps lenses clean.
- cleadew can be used for all soft contact lenses.

1970s to 1980s

Heat disinfection



1991

Hydrogen peroxide-based solution

(Disinfection solution+ Neutralization solution)



Launch of chemical disinfectants in the market

1996

Hydrogen peroxide-based solution

(Disinfection liquid solution + Platinum disc)



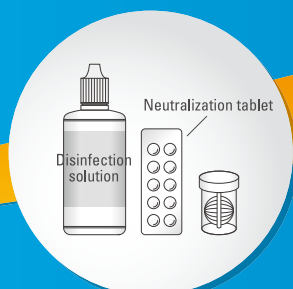
Multi-purpose solution (MPS)



2001

Hydrogen peroxide-based solution

(Disinfection solution + Neutralization tablet)



Further progress!

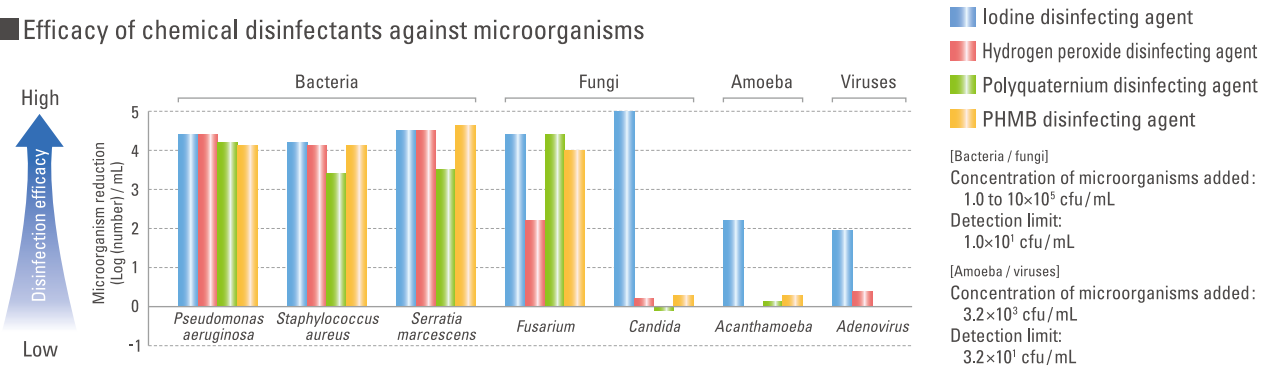


## Povidone iodine is a fast-acting disinfectant with a wide antibacterial spectrum.

Povidone iodine exhibits much stronger disinfection efficacy against bacteria, fungi, viruses, and acanthamoeba as compared with other disinfectants.

Efficacy of each disinfectant against bacteria, fungi, viruses, and amoeba were compared according to the stand-alone test.\*1

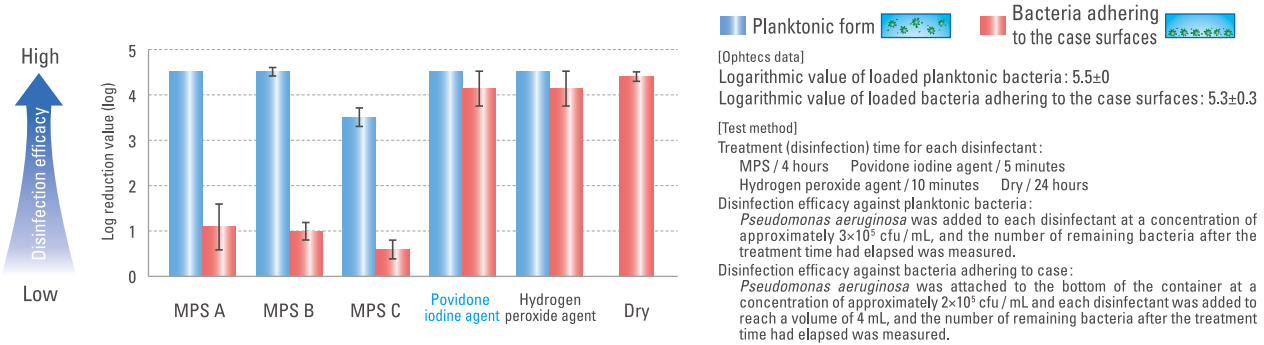
### Efficacy of chemical disinfectants against microorganisms



Kiichi Ueda, Ryoji Yanai "Silicone hydrogel contact lenses and multi-purpose solution, eye drops" (Journal of the Eye 25: 923 - 930, 2008)

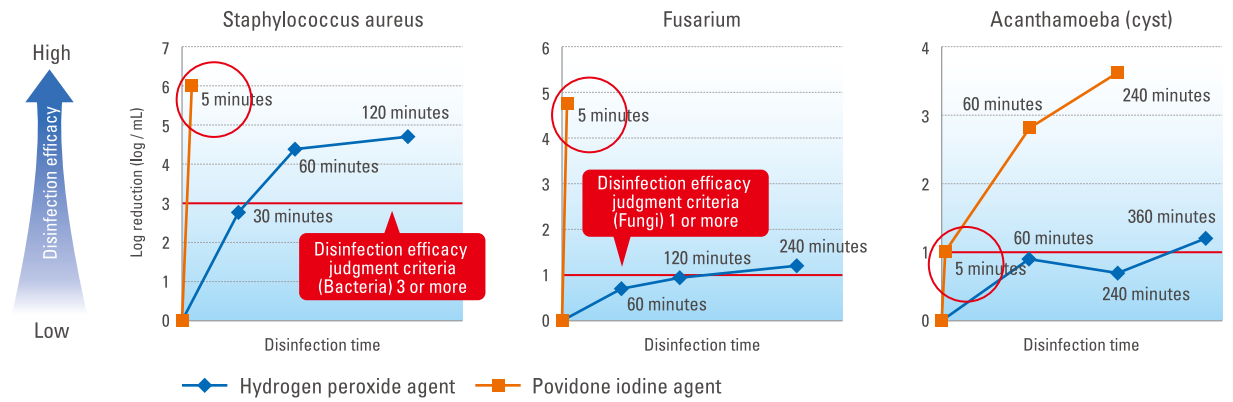
## Povidone iodine is also effective for biofilm which is disputed as a causative factor for infection.

Efficacy of each disinfectant against both 'free-floating' and 'adherent to the case' of *Pseudomonas aeruginosa* were evaluated. The povidone iodine agent was found to exhibit a high disinfection efficacy against bacteria adhering to the case surfaces which is more disinfectant-resistant.



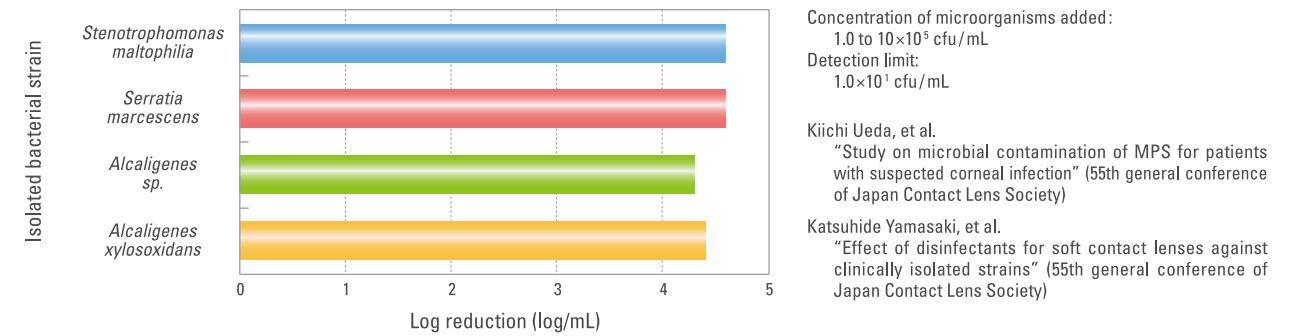
## The povidone iodine agent exhibits immediate effect against various microorganisms.

The disinfection efficacy against various microorganisms were evaluated over time using the povidone iodine agent and hydrogen peroxide. The povidone iodine agent was proven to exhibit immediate effect even against amoeba cysts, which are resistant to disinfection as well as against bacteria and fungi.



## The povidone iodine agent also exhibits a strong disinfection efficacy against bacteria caused by secondary pathogenic bacteria in the MPS bottle.

The povidone iodine agent was confirmed to have a strong disinfection efficacy against bacterial strains isolated from the MPS bottle in the stand-alone test.\*1



\*1 Stand-alone test: Add the five designated strains (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Fusarium*, *Candida albicans*) to the disinfectants, at concentrations ranging from 1.0×10<sup>5</sup> cfu/mL to 1.0×10<sup>6</sup> cfu/mL, to evaluate the decrease in the number of microorganisms as a log reduction\*2 after the time prescribed for each disinfectant. If the results represented as log reduction values exceed 3 (in the case of bacteria) or 1 (in the case of fungi), the disinfectant is judged to be effective.

\*2 Log reduction: Indicates the degree of decrease in the number of microorganisms after disinfection as compared with the number of initially added microorganisms as a logarithmic value.

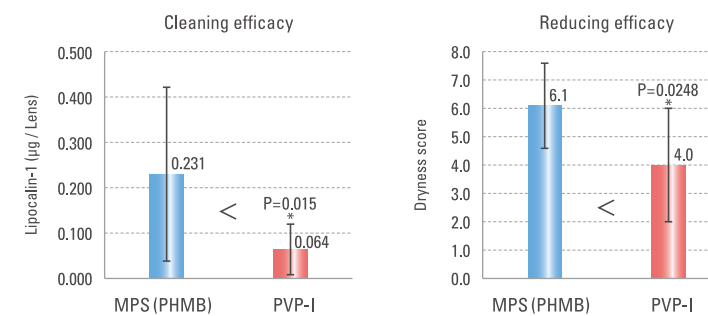


## The proteolytic enzyme completely removes daily deposits.

cleadew is a proteolytic enzyme-containing disinfectant for soft contact lenses.\* It consistently removes protein on the lens at each application. \*As of January, 2013

PVP-I system showed higher cleaning efficacy on lipocalin-1 and there was significant reduction of dryness symptoms in comparison with MPS.

### Cleaning efficacy on lipocalin deposited on silicone hydrogel lenses and reduction of dryness



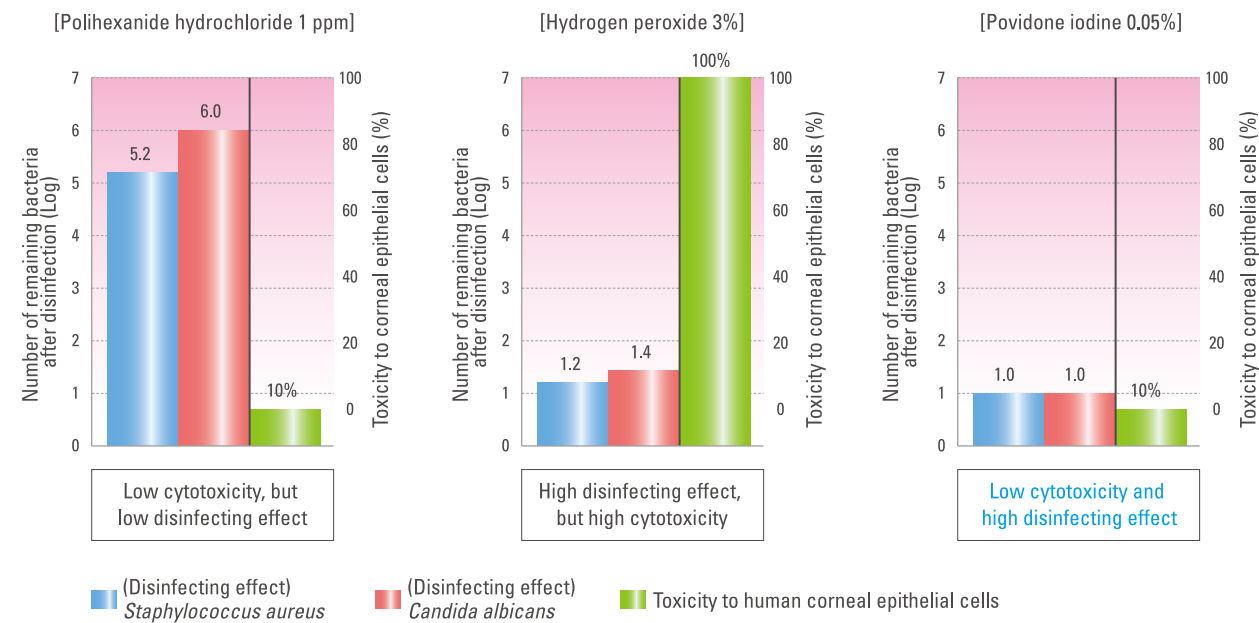


# Safety

## Povidone iodine is a disinfectant with low cytotoxicity and little eye irritation.

**Povidone iodine at a concentration prescribed for cleadew not only has a high disinfecting effect but also low cytotoxicity.**

Polihexanide hydrochloride, hydrogen peroxide, and povidone iodine were compared at their concentrations prescribed as disinfectants for soft contact lenses with respect to the disinfecting effects against *Staphylococcus aureus* and *Candida albicans* and the damage to human corneal epithelial cells. The results confirmed that 0.05% povidone iodine, a concentration prescribed for cleadew, has not only low cytotoxicity but also a high disinfecting effect.



[Test method]  
 Treatment (disinfection) time for each disinfectant: MPS / 4 hours, povidone iodine agent / 5 minutes, hydrogen peroxide / 10 minutes  
 Disinfecting effect: The number of remaining bacteria after the treatment time had elapsed was evaluated according to the ISO stand-alone test.  
 Cytotoxicity: After human corneal epithelial cells had been cultivated on the bottom surface of the container and 4 mL of each disinfecting agent placed in contact with the cells, the number of remaining bacteria was evaluated.

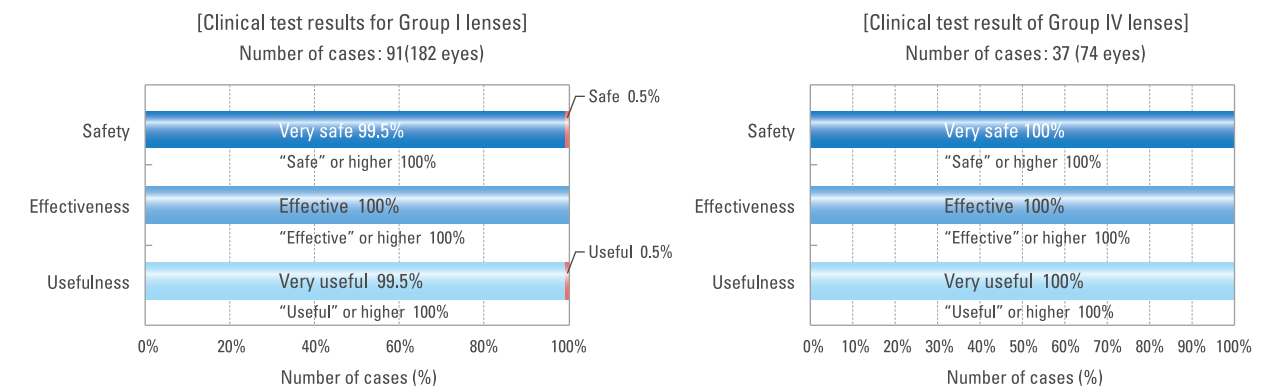
Ryoji Yanai, et al. "Evaluation of povidone-iodine as a disinfectant solution for contact lenses: Antimicrobial activity and cytotoxicity for corneal epithelial cells" Contact Lenses & Anterior Eye 29 (2006) 85 - 91

# Clinical Data

## Povidone iodine agent evaluated as being useful as a disinfectant.

**Povidone iodine agent proved to be very safe and useful as a disinfectant without severe side effects for contact lenses of Group I and Group IV.**

An open test was conducted using contact lenses of Group I and Group IV for 6 months (Group I) and for 12 weeks (Group IV) to evaluate the safety, effectiveness, and usefulness of povidone iodine.



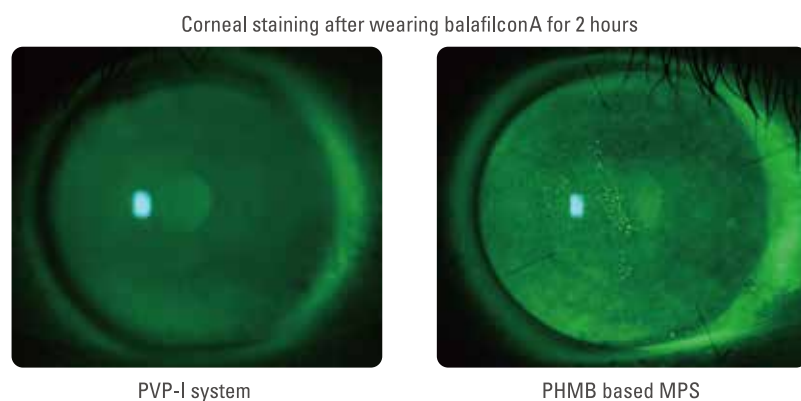
[Evaluation method] Comprehensive evaluation judgment criteria

- Effectiveness:** To be judged based on the infection possibility score at each measurement point
  - 1. Very effective Total score is 0.
  - 2. Effective Total score is 1.
  - 3. Neither effective nor ineffective Total score is 2 and the test is continued.
  - 4. Ineffective Total score is 2 and the test is discontinued. Or, Total score is 3 or more.
- Safety:** To be judged based on the score for side effects at each measurement point
  - 1. Very safe Total score of 1 or less.
  - 2. Safe Each score of 1 or less.
  - 3. Slight issue Some scores of 2
  - 4. Not safe Some scores of 3
- Usefulness:** Lower-level judgment to be adopted among those for the usefulness and the safety evaluation
  - 1. Extremely useful
  - 2. Useful
  - 3. Questionable in terms of usefulness
  - 4. Undesirable

Takamasa Matsuda, et al., "Clinical evaluation of new soft contact lenses disinfection system OPL 7 (Test using Group I lenses) Folia Ophthalmologica Japonica 52: p687 - 701, 2001  
 Yuko Sugie, et al., "Clinical evaluation of new soft contact lenses disinfection system OPL 7 (Test using Group IV lenses) Folia Ophthalmologica Japonica 52: p702 - 713, 2001

## 0.05% povidone iodine has minimal adverse effects on the cornea.

Treat balafilconA lenses with PVP-I system and MPS respectively. 16 hours later, wore the lenses and observed 2 hours later.

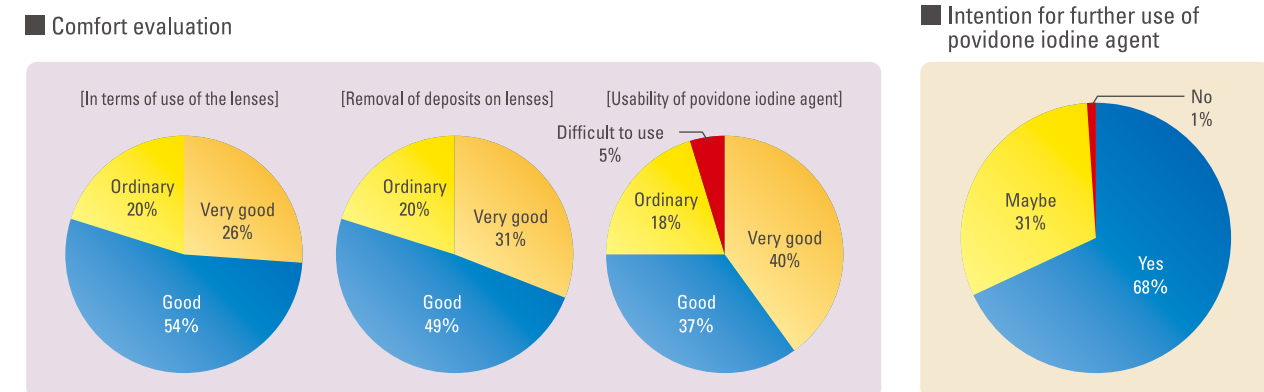


[Test method]  
 PVP-I system did not show corneal staining which was seen when used PHMB based MPS

[In-house document]

## The povidone iodine agent was evaluated as good in terms of use by 80% subjects in the clinical research on silicone hydrogel lenses, and 70% of subjects expressed intent to continue use.

65 subjects were divided into 4 groups, and each group used povidone iodine agent and different silicone hydrogel lenses for 3 months.



• No significant differences in objective opinions and subjective symptoms between the lenses

Kiichi Ueda, et al., "Clinical trial of povidone iodine agent OPL 78 for silicone hydrogel lenses" (Journal of the Eye 27: 1310 - 1317, 2010)