

SUMMARY OF SAFETY AND EFFECTIVENESS

I. General Information

- A. **Device Generic Name:** purified polydimethylsiloxane (ProCode LWL - Intraocular Fluid)
- B. **Device Trade Name:** SILIKON 1000 (purified polydimethylsiloxane)
- C. **Applicant's Name and Address:**

Richard-James, Inc.
2 Centennial Drive
Peabody, MA 01960
- D. **Investigational Device Exemptions (IDE) Number:** G900075
- E. **Date of Panel Recommendation:** January 13, 1997
- F. **Premarket Approval Application (PMA):** P950008
Date Filed: February 22, 1995
Date Approved: September 25, 1997
- G. **GMP Inspection:** May 20, 1997
- H. **Date of Notice of Approval to Applicant:** September 25, 1997

II. Indications for Use

SILIKON 1000 is indicated for use as a prolonged retinal tamponade in selected cases of complicated retinal detachments where other interventions are not appropriate for patient management. Complicated retinal detachments or recurrent retinal detachments occur most commonly in eyes with proliferative vitreoretinopathy (PVR), proliferative diabetic retinopathy (PDR), cytomegalovirus (CMV) retinitis, giant tears, and following perforating injuries. SILIKON 1000 is also indicated for primary use in detachments due to Acquired Immune Deficiency Syndrome (AIDS) related CMV retinitis and other viral infections affecting the retina.

III. Contraindications

As silicone oil can chemically interact with and opacify silicon elastomers, the use of SILIKON 1000 is contraindicated in pseudophakic patients with silicone intraocular lenses. Use of SILIKON 1000 is contraindicated in patients with a known hypersensitivity to silicone oil.

IV. Warnings and Precautions

The warnings and precautions can be found in the labeling (Attachment 1).

V. Device Description

SILIKON 1000 is a sterile, highly purified long chain polydimethylsiloxane. It is a clear colorless liquid at room temperature with a nominal viscosity of 1000 centistokes (cs). SILIKON 1000 (purified polydimethylsiloxane) or α -(Trimethylsilyl)- ω -methylpoly[oxy(dimethylsilylene)] is a copolymer, having an average molecular weight of approximately 44,000, and is synthesized from dichlorodimethylsilane and chlorotrimethylsilane. SILIKON 1000 has a high surface tension (>21 dynes/cm) and is immiscible with aqueous components. It has the following formula:



It has a specific gravity between 0.96 and 0.98 g/cm³ (25°C) and a refractive index between 1.402 and 1.405 (25°C). Low molecular weight siloxanes are $\leq 0.0200\%$ (200 ppm) for each detectable cyclic or linear species. Terminal -OH end groups do not exceed 100 ppm. Each 1 mL contains solely polydimethylsiloxane oil in neat form.

SILIKON 1000 has the following physical and chemical specifications for finished product:

Specifications:

Viscosity (25°C)	900 - 1200 cs
Polydispersity (MW/MN)	< 2.5
Volatility (TGA @ 200°C)	< 1.0%
Volume resistivity	> 1 x 10 ¹³ Ohm cm
Low Molecular Weight Cyclic Siloxanes	≤ 200 ppm each
Weight Average Molecular Weight	38,000 - 48,000
Particulate matter (particules/ml)	≤ 50 @ ≤ 10 μm; ≤ 5 @ ≤ 25 μm
FT-IR	Complies to USP
Acidity	< 0.10 ml
Heavy Metals limit test	< 0.001 %
Sterility (USP)	Sterile
Bacterial endotoxins	≤ 0.5 EU/mL

SILIKON 1000 is supplied in 10 mL glass vials filled with 8.5mL of sterile silicone oil.

VI. Alternative Practices and Procedures

Silicone oil is used as a postoperative tamponade following vitreous surgery in cases of complicated retinal detachment either when previous attempts to reattach the retina have failed, or when the condition of the eye or of the patient makes surgery with alternative practices unlikely to succeed.

Conventional retinal surgery for retinal detachments consists of scleral buckle surgery (Custodis 1953, Schepens 1964, and Lincoff et al. 1965), sometimes accompanied by external drainage of subretinal fluid through a sclerotomy, and cryotherapy or laser photocoagulation of the edges of the retinal tears (Meyer-Schwickerath 1959 and Lincoff et al. 1964). These procedures are effective in most cases of primary retinal detachment. Some cases of retinal detachment present with conditions that make scleral buckling surgery less effective such as: posteriorly located retinal breaks, significant scar tissue on the surface or underneath the retina which exerts traction on the retina preventing reattachment, or optical problems which obstruct the view of the retina. In detachments complicated by these conditions, many such eyes can be treated successfully with vitrectomy techniques, during which the retina is repositioned into its normal location by endodrainage of subretinal fluid through holes in the retina during an exchange of the normal intraocular fluid contents for either air, or a long- acting gas (Fineberg et al. 1975, Machemer and Laqua 1978, Abrams et al. 1982, and Lucke and Laqua 1990).

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Following initially successful retinal detachment surgery, intraocular scar tissue can proliferate to an extent that the scar tissue exerts enough traction on the retinal surface to cause retinal redetachment. This condition is called proliferative vitreoretinopathy (PVR). In order to repair detachments with significant amounts of PVR, the scar tissue must be peeled off of the retina (Machemer and Laqua 1978, Michels 1981, and Charles 1981). Following this membrane peeling, the retina is repositioned and the vitreous cavity is filled with an agent to act as a tamponade to keep the retina in its normal position while a chorioretinal scar is forming induced by photocoagulation or cryotherapy of the retina surrounding retinal tears. Various gas tamponades are used, such as perfluoropropane and sulfurhexafluoride (Lincoff et al. 1983, and Faulbourn and Bowald 1987). These intraocular gas bubbles gradually decrease in size. As the bubbles decrease in size, it becomes imperative that patients position their heads in order to keep the gas bubble opposed to the areas of the retinal breaks. If the retinal tears are inferior, the patient often must maintain strict face-down positioning for extended periods of time.

VII. Dosage and Administration

The Dosage and Administration of SILIKON 1000 can be found in the labeling under "Directions for Use" (Attachment 1).

VIII. Marketing History

SILIKON 1000 has not been marketed in the United States as an intraocular fluid.

IX. Potential Adverse Effects

The data supporting the rates of occurrence of adverse reactions were derived from the sponsored prospective U.S.-based multicenter clinical trial (2754 total eyes treated with 2573 Core Study eyes analyzed at 36 investigational centers), consisting of 757 CMV and 1816 non-CMV (PDR, Giant Tear, PVR and Trauma and 181 "other" diagnoses related retinal detachments which are not represented in the Core Study analyses). Comparative data from two other published studies conducted by other sponsors with silicone oils were considered in the analysis of safety and effectiveness. These included, (1) the National Eye Institute Silicone Study Group (Silicone Study Reports #1 and #2) and (2) the Lucke Study (Lucke K., Laqua H: *Silicone Oil in the Treatment of Complicated Retinal Detachments*, Springer-Verlag, Berlin, 161 pages, 1990).

The percentages reported below represent the range of occurrence for the SILIKON 1000 prospective study.

Table 1 - 6 Months and Last Examination for Safety Outcomes

OUTCOME	VISIT ¹	CMV	Non-CMV
Emulsification in eyes w/oil	6 month	1%	3%
	Last visit	1%	3%
Cataract in phakic eyes	6 month	64%	63%
	Last visit	38%	71%
Hypotony*	6 month ²	6%	19%
	Last visit	4%	19%
Elevated IOP	6 month ³	0%	3%
	Last visit	1%	5%
Corneal opacity/abrasion*	6 month ⁴	6%	26%
	Last visit	4%	31%

* The rate of previous vitreoretinal operative procedures was 14% for CMV patients and 86% for non-CMV patients.

¹ The last visit may have occurred anytime post-operatively, and the 6 month visit may have occurred post-operatively between 137 and 272 days.

² Incidence rate of hypotony in non-CMV subjects at 6-months postoperatively was significantly greater in aphakic (21%) and pseudophakic (17%) eyes versus phakic (7%) eyes ($p < 0.01$).

³ Incidence rate of elevated IOP in non-CMV subjects at 6-months postoperatively was significantly greater in phakic eyes (7%) versus aphakic (3%) and pseudophakic (2%) eyes ($p = 0.03$).

⁴ Incidence rate of corneal opacity/abrasion in non-CMV subjects at 6-months postoperatively was significantly greater in aphakic (30%) and pseudophakic (21%) eyes versus phakic (8%) eyes ($p < 0.01$). Incidence rate of corneal opacity/abrasion in CMV subjects at 6-months postoperatively was significantly greater in aphakic (20%) and pseudophakic (11%) eyes versus phakic (4%) eyes ($p=0.04$).

Table 2 provides the safety and efficacy results at 6, 12, and 24 months stratified by complete attachment and macula attachment for Company A.