

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Mr. Daniel J. Manelli
Consultant for Lobob Laboratories, Inc.
Farkas & Manelli, P.L.L.C.
2000 M Street N.W.
Suite 700
Washington, DC 20036-3307

APR 30 1998

Re: P940025
Lobob W/RW Drop
Filed: May 23, 1995
Amended: May 25, June 9, July 17, and August 2, 1995; and
March 26, May 7, November 5 and 15, 1996; and April 21, 1998

Dear Mr. Manelli:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of the premarket approval application (PMA) that you submitted on behalf of Lobob Laboratories, Inc., for the Lobob W/RW Drop. This device is indicated for use to wet fluoro-silicone acrylate and silicone acrylate rigid gas permeable contact lenses prior to insertion and to lubricate lenses while they are on the eye. Your client may begin commercial distribution of the device upon receipt of this letter.

Expiration dating for this device has been established and approved at 18 months for the 1 fl. oz. (30 ml) and 12 months for the 0.3 fl. oz. (10 ml) bottle sizes. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(8).

CDRH will notify the public of its decision to approve the PMA by making available a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/cdrh/pmapage.html>. Written requests for this information can also be made to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., Rm. 1-23, Rockville, MD 20857. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Effective July 7, 1997, CDRH reclassified contact lens care products from class III (premarket approval) to class II (special controls). Although the device is subject to the reclassification order, CDRH continued to process this application as a PMA to facilitate approval since the only outstanding issue at the time of reclassification was compliance with the Good Manufacturing Practice Regulation. This issue was subsequently resolved on April 30, 1998.

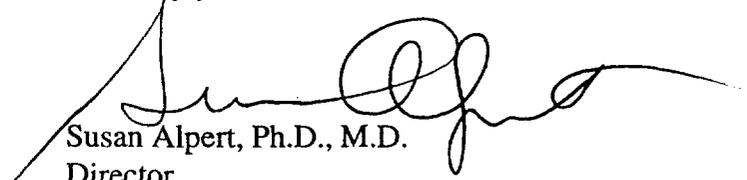
Future modifications of the device are subject to the premarket notification (510(k)) provisions of the act. Guidance for preparing a 510(k) submission is found in the "Guidance for Industry, Premarket Notification (510(k)) Guidance Document for Contact Lens Care Products" dated May 1, 1997, which can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/cdrh>. You may obtain a hard copy of the guidance by faxing your request to the Division of Small Manufacturers Assistance [fax (301) 443-8818].

All correspondence regarding 510(k) submission should be submitted to the address below:

510(k) Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Ms. Muriel Gelles or James F. Saviola, O.D., at (301) 594-1744, or Kathy Poneleit at (301) 594-2186.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Susan Alpert", with a long horizontal flourish extending to the right.

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Summary of Safety and Effectiveness Data

I. General Information

- A. Device Generic Name: sterile lubricating and wetting solution for use with fluoro-silicone acrylate and silicone acrylate rigid gas permeable contact lenses
- B. Device Trade Name: Lobob W/RW Drop
- C. Applicant's Name and Address: Mr. Daniel J. Manelli
Consultant
Lobob Laboratories, Inc.
1440 Atteberry Lane
San Jose, CA 95131
- D. Premarket Approval Application (PMA) Number: P940025
- E. Date of Notice of Approval to Applicant: APR 30 1998

II. Indications

Lobob W/RW Drop is indicated for use to wet fluoro-silicone acrylate and silicone acrylate rigid gas permeable contact lenses prior to insertion and to lubricate lenses while they are on the eye.

III. Device Description

Lobob W/RW Drop is a sterile solution containing sodium and potassium chloride salts, polyvinyl pyrrolidone, polyvinyl alcohol, hydroxyethylcellulose, sodium bisulfite 0.02%, and preserved with benzyl alcohol 0.1%, sorbic acid 0.05%, and edetate disodium 0.1%.

IV. Center for Devices and Radiological Health (CDRH) Decision

The application includes by reference the data in P870029 for STAY-WET 3^R and all related supplements that led to the approval of STAY-WET 3^R, submitted by Sherman Laboratories, Inc. and approved by FDA on March 31, 1989. Sherman Laboratories, Inc. has authorized Lobob Laboratories, Inc. to incorporate by reference the information contained in its approved PMA to manufacture the device.

CDRH approval of Lobob Laboratories, Inc.'s PMA is based on (1) the safety and effectiveness data contained in PMA P870029 and related supplements and (2) the results of the FDA inspections of the manufacturing facilities. A summary of safety and effectiveness data for the STAY-WET 3^R appears in Attachment A.

Effective July 7, 1997, CDRH reclassified contact lens care products from class III (premarket approval) to class II (special controls). Although the device is subject to the reclassification order, CDRH continued to process this application as a PMA to facilitate approval since the only outstanding issue at the time of reclassification was compliance with the Good Manufacturing Practice Regulation. This issue was subsequently resolved on APR 30 1998.

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices Panel for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel. CDRH approved this application and final labeling on APR 30 1998.

The device shelf-life has been established and approved as 18 months.

V. Potential Adverse Effects of the Device on Health

Potential adverse effects on health resulting from the use of this device are listed in the package insert under "ADVERSE REACTIONS (PROBLEMS AND WHAT TO DO)" (Attachment B).

VI. Conditions of Approval

CDRH has determined that no special restrictions or conditions pertain other than those described in the "Conditions of Approval" enclosed with the approval order. A copy of the approved draft labeling is attached (Attachment B).

Attachments A and B

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Summary of Safety and Effectiveness Data

I. General Information

- A. Device Generic Name: sterile lubricating and wetting solution for use with silicone acrylate rigid gas permeable contact lenses
- B. Device Trade Name: STAY-WET 3®
- C. Applicant's Name and Address: Sherman Laboratories, Inc.
P.O. Box 368
Abita Springs, Louisiana 70420
- D. Premarket Approval Application (PMA) Number: P870029
- E. Date of Panel Recommendation: June 21, 1988
- F. Date of Notice of Approval to Applicant: MAR 31 1989

II. Indications

STAY-WET 3® is indicated for use to wet silicone acrylate rigid gas permeable (RGP) contact lenses prior to insertion and to lubricate lenses while they are on the eye.

III. Device Description

STAY-WET 3® is a sterile solution containing sodium chloride, potassium chloride, polyvinyl pyrrolidone (PVP), polyvinyl alcohol (PVA), hydroxyethylcellulose and sodium bisulfite 0.02%, preserved with benzyl alcohol 0.1%, sorbic acid 0.05% and edetate disodium 0.1%.

IV. Alternative Practices or Procedures

Alternative practices or procedures available to the patient are the use of other commercially available solutions for the same indications.

V. Summary of Studies

A. Preclinical:

1. Toxicology: The applicant conducted the battery of tests outlined in "Toxicology Guidelines" section of the Class III Contact Lens Product Guideline, an FDA guideline dated May 1983. In addition to the guideline testing, the applicant provided the following toxicology information for the preservative, benzyl alcohol:

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- a. guinea pig maximization test was conducted to assess the sensitization potential of benzyl alcohol
- b. Cochet-Bonett Test was conducted on humans to determine the possible anaesthetic effect of benzyl alcohol to the cornea
- c. corneal penetration test was conducted in rabbits to determine the adsorption and distribution in ocular tissue and to determine if benzyl alcohol is metabolized during corneal penetration
- d. corneal epithelial wound healing study was conducted in rabbits to determine if benzyl alcohol had any effect on the rate of epithelial wound healing
- e. Product Safety Information Sheet containing the following information:
 1. the acute oral LD50 is 1230 mg/kg to 3100 mg/kg in rats
 2. the acute oral LD50 is 1580 mg/kg in mice
 3. the acute oral LD50 is 1040 mg/kg in rabbits
 4. the acute dermal LD50 is 2000 mg/kg in rabbits
 5. the acute inhalation LC50 is 1000 ppm in rats after an 8-hour inhalation exposure
 6. benzyl alcohol meets the requirements of the Federal OSHA Hazard Communication Standard (29 CFR 1900.1200)

Conclusion:

The results from the guideline testing for the device along with the additional testing described above provide reasonable assurance that the solution and its preservatives, benzyl alcohol, at the concentration proposed for use (0.1%), and sorbic acid, raise no acute toxicological concerns and support the safety of the device for its intended use as stated in the approved labeling. The safety of sodium bisulfite has been established as safe for use in ophthalmic solutions as listed in the OTC ophthalmic monograph. The labeling contains adequate warning regarding the use of the product by persons with sensitivities to the ingredient such as asthmatics and contraindicates use of the device by persons allergic to any ingredients in the solution with special emphasis placed on asthmatic persons.

2. Microbiology: The applicant conducted the battery of tests outlined in "Microbiology Guidelines" section of the Class III Contact Lens Product Guideline, an FDA guideline dated May 1983.

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Conclusion:

The results from these tests provide reasonable assurance that the solution remains sterile as packaged for at least 36 months.

3. Lens/Solution Compatibility: The applicant conducted tests to establish that the solution does not adversely affect lens color, base curve, diameter, center thickness, and power. In these tests, 5 Polycon, 5 Polycon II, 1 Boston IV, 4 Paraperm O₂ Plus, and 5 Optacryl K lenses were cycled through 30 cleaning and disinfection cycles. The lenses were then examined to determine the effect of the test solution on the lenses. There were no changes in lens color and parameters.

Conclusion:

The results from these tests provide reasonable assurance that the solution is compatible with clear and tinted silicone acrylate rigid gas permeable contact lenses.

4. Solution Stability: The applicant conducted tests to establish the stability of the solution and the appropriate expiration dating. The test solution was packaged into the finished product containers stored at various temperatures, and examined for conformance to original specifications.

Conclusion:

The results from these tests provide reasonable assurance that the solution remains stable as packaged for at least 36 months in its 1 fl. oz. (30 mL) container.

5. Preservative Uptake/Release: A preservative uptake/release study was conducted by the applicant for benzyl alcohol and sorbic acid. Two lenses each of Polycon, Polycon II, Boston II, Paraperm O₂ Plus, and Optacryl K silicone acrylate rigid gas permeable contact lenses were soaked in the solution, and the uptake and release of benzyl alcohol and sorbic acid was measured in accordance with the FDA Guidelines dated May 1983.

Conclusion:

The results from these tests demonstrate minimal risk to patients from uptake and release of the preservatives by silicone acrylate rigid gas permeable contact lenses and supports the safety of the device for its intended use when accompanied by appropriate labeling. The labeling for the device contraindicates use of the device by persons allergic to any ingredients in the solution. In addition, the labeling for the device warns that the solution is not to be used directly in the eye.

6. **Wetting Effectiveness:** The applicant conducted an in vitro contact angle study to assess the effectiveness of Stay Wet 3[®] in the wetting of silicone acrylate RGP lenses. Using 1 each of Boston II, Paraperm O₂ Plus and Polycon II silicone acrylate lenses, contact angle measurements were taken using the Captive Bubble method. Lenses were treated with Stay Wet 3[®], submerged in saline solution at 25° C, and suspended with the front curve down. A bubble of air was released below the lens and trapped on the front curve. The angle of contact between the bubble and the lens surface was measured in degrees using a Gonimeter. Initially after treatment with Stay Wet 3[®] (zero time), the lenses were very wettable and the bubble would not adhere to the lens surface. Measurements could only be performed on the treated lenses after 5 minutes equilibration time in the saline; therefore, the 5 minute time was used as the baseline measurement. Measurements were also provided at the 15 minute and 30 minute intervals to determine if the wettability effect would last for a sustained period of time; i.e., at least 30 minutes. Results were as follows:

Contact Angle by Time Measured in Degrees

<u>Lens</u>	<u>5 minutes</u>	<u>15 minutes</u>	<u>30 minutes</u>
Boston II	19	20	21
Paraperm O ₂ Plus	20	20	22
Polycon II	19	21	22

Conclusion:

The results from this study indicate that the wettability effect of the device as determined by the contact angle measurements was immediate and remained essentially unchanged for at least 30 minutes when compared to baseline measurements (5 minutes). The results provide supporting evidence that the device is effective in wetting silicone acrylate RGP lenses.

7. **Additional Information:** The applicant offered additional information to provide support of the effectiveness of the preservative, benzyl alcohol. This information includes references to USP XXI (page 1195) which lists benzyl alcohol as one of the commonly used antimicrobial agents and to United States Dispensatory, 26th Edition, (page 198) which lists benzyl alcohol as having bacteriostatic effects.

Conclusion:

The information cited above provides additional supportative evidence of the effectiveness of benzyl alcohol as an antimicrobial agent.

B. **Clinical:**

The purpose of the clinical study was to evaluate the safety and effectiveness of the device in accordance with the proposed labeling.

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The clinical study was conducted in accordance with the "Clinical Guidelines" section of the Class III Contact lens Product Guidelines, an FDA guideline dated May 1983.

Patient Selection Criteria

The patients enrolled into this clinical study were to meet the following criteria:

1. be willing to adhere to the regimen of hygiene prescribed;
2. have normal eyes as defined in the protocol and use no ocular medications; and
3. have need of an optical correction.

Study Population

A total of 228 patients (451 eyes) was enrolled by 9 investigators into this clinical study. There were 148 females and 80 males ranging in age from 7 years to 73 years. Of the 228 patients (451 eyes) enrolled into the study, 213 patients (423 eyes) completed the 6-month study, and 15 patients (28 eyes) were discontinued from the study as discussed on page 9 of this summary. All patients in the study used STAY-WET 3® and de-STAT 3® (a cleaning, storage and conditioning solution which is the subject of another PMA). Lenses worn during the study were:

<u>Lenses</u>	<u>No. of Eyes</u>
Optacryl and Optacryl K	126
Boston II	124
Paraperm	57
Polycon and Polycon II	50
Silcon	44
Optacryl 60	32
Ultraflex	4
Flex	4
Airlens	2
B.P. Flex	2
Bioflex	2
GP II Hydrocurve	2
Ellipsecon	2

Study Period

The clinical study began on March 8, 1984, and ended on April 16, 1985. The study period was 6 months.

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Findings

1. Safety:

Adverse Reactions

In evaluating this device, an adverse reaction was considered to be a serious, vision-threatening problem that was unanticipated, but which might have been attributed to the use of the study device. There were no adverse reactions reported during the course of this clinical study.

Slit Lamp Findings

A positive slit lamp finding is considered to be a routinely occurring complication that would be expected with or without the presence of contact lenses and with or without the use of the study device. The degree of severity can range from very slight to serious. At the least severe, the findings present no medical concerns and are noticeable only by microscopic slit lamp examination. In a severe state, the findings require medical treatment.

Slit lamp examinations were performed initially and periodically throughout the study. The applicant used the classification of slit lamp findings as outlined in attachment A. Positive slit lamp findings for the 423 eyes completing the study were as follows:

<u>Slit Lamp Finding</u>	<u>Initial Visit 423 eyes</u>	<u>Follow-up Visits 2,526 eyes</u>	<u>Final Visit 423 eyes</u>
Edema			
Grade 1	0	1	0
Injection			
Grade 1	0	7	0
Staining			
Grade 1	2	49	9
Grade 2	0	4	0
Grade 3	2	2	0
Grade 4	0	5	0
Grade 5	0	1	1
Grade 8	0	1	1
Iritis	0	0	0
Vascular- ization			
Grade 1	0	4	0
Other	0	0	0

One patient had recurrent grade 3 staining in both eyes at the initial and 2-week visits. The condition resolved as the study progressed.

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There were 5 reports of grade 4 staining (diffuse superficial punctate staining), 2 reports of grade 5 staining (epithelial dimpling associated with gas bubbles under the lens), and 2 reports of grade 8 staining (foreign body track staining) during the study. In each case the findings resolved with no sequelae, and all patients successfully completed the study.

Conclusion:

There were no positive slit lamp findings requiring medical treatment during this study. The positive slit lamp findings in this clinical study are within expected limits for contact lens wear and do not raise any significant concerns regarding the safety of the device when used as directed in the approved labeling.

Patient Symptoms, Problems and Complaints

Patient symptoms, problems and complaints were reported by the investigators during the clinical study. Of the 3,872 eye examinations conducted, a total of 2,971 eye examination reports were provided for patient symptoms, problems and complaints during the course of the 6-month study. Patient symptoms, problems and complaints (multiple reports) were reported as follows:

	<u>No. Reports</u> <u>All Visits</u>
Awareness of lens	13
Excessive blink rate	8
Variable vision	8
Lenses need cleaning	8
Pain, burning, itching	5
Excessive movement	5
Spectacle blur	4
Handling problems	4
Reading problems	4
Flare	3
Excessive tearing	3
Distance vision blurred	2
Eyes clouded up	2
Dry eyes	2
Scratching	2
Tired eyes	2
Eyes feel swollen	2
Discomfort	1
Excessive blink rate and movement	1

Conclusion:

The patient symptoms, problems and complaints reported during this study were within expected limits for contact lens wear and do not raise any significant concerns about the safety or effectiveness of the device.

2. Effectiveness:

Visual Acuity

For the 423 eyes completing the study, visual acuity with lenses was reported as 20/30 or better for 407 of 415 eyes at the initial visit and 419 of the 421 eyes at the final visit. Visual acuity was not reported for 8 eyes at the initial visit and 2 eyes at the final visit. Visual acuity data was provided for the initial visit and was compared to visual acuity at the last visit. Results for the completer eyes were:

<u>Visual Acuity</u>	<u>Initial Visit (423 eyes)</u>	<u>Final Visit (423 eyes)</u>
20/20 or better	372	405
20/25	26	14
20/30	9	0
20/40	6	0
20/50	0	0
20/60	1	1
20/150	0	1
20/200	1	0
Not reported	8	2

Conclusion:

There were no decreases in visual acuity greater than 1 Snellen line. A fluctuation in visual acuity of 1 Snellen line is not unusual for a contact lens and contact lens solution study due to measuring techniques and normal fluctuation and is not significant in terms of visual acuity. The visual acuity results in this clinical study do not raise any significant concerns regarding the safety and effectiveness of the device and provide reasonable assurance that the device does not adversely affect the lenses.

Lens Wearing Time

The average daily lens wearing time ranged from 14 hours at the 2-week visit to 15.3 hours at the final visit.

Conclusion:

The lens wearing times reported for this study provide reasonable assurance that most patients were wearing their lenses for at least 14 hours each day without negative effects from the use of the device.

Discontinued Patients

There were 15 patients (28 eyes) discontinued from this study. Reasons for discontinuation were:

<u>Reason</u>	<u>No. Eyes</u>
Lost-to-follow-up	20
Moved	4
Discomfort	2
Failure to comply with instructions	2

There were no eyes discontinued for reason of pathology. All eyes discontinued from the study were discontinued by the 8-week visit.

Conclusion:

The reasons for and incidence of discontinuance in this clinical study are within expected limits for contact lens wear and do not raise any significant concerns regarding the safety and effectiveness of the device.

Lens Replacements

There were 34 lenses replaced during this clinical study. Reasons reported for replacements were as follows:

<u>Reason</u>	<u>No. of Lenses</u>
Acuity	11
Back-up lenses	10
Lost	4
Spectacle blur	2
Physiology and fitting	2
Not specified	2
Comfort	1
Fitting	1
Warpage	1

"Physiology and fitting" was reported as grade 1 edema and lens parameter change.

Conclusion:

The reasons for lens replacements in this study are within expected limits for contact lens wear. These reasons and numbers of replacements do not raise any significant concerns about the safety and effectiveness of the device.

Wetting and Lubricating Evaluation

At the 6-month visit the 213 patients completing the study were asked to evaluate the subject device. Vision was reported as very good by 205 patients and acceptable for 8 patients; comfort was very good for 206 patients and acceptable for 7 patients; and physiology response (slit lamp findings) was reported as very good for 206 patients and acceptable for 7 patients.

Of these 213 patients 155 patients experienced improved wetting of their lenses compared to the wetting solution previously used and 149 patients indicated that the subject device was less irritating than their previous lubricating solution.

One year after completion of the study patients were asked to evaluate the subject device. Of the 213 patients completing the study, responses were received from 164 patients. Of these, 155 patients reported that lens wetting was improved, 149 patients reported that the subject device was less irritating than their previous lubricating and wetting solution, and 156 patients were more satisfied with the subject device than with their previous lubricating and wetting solution.

All patients completing the study used the subject device as directed prior to lens insertion. The device was used as a lubricating and rewetting solution twice each day for 26 patients and once each day for 70 patients. Because patients were instructed to use the device for lubricating and rewetting as needed the solution was not used as a lubricant by 69 patients that did not experience dry eyes. Use of the solution was not reported for 48 patients. However, the absence of adverse reactions and the relatively low reports of positive slit lamp findings indicates there were no negative reports by these 48 patients.

Conclusion:

Based upon the clinical experineces cited above and the ingredients of the device which are listed in the OTC monograph as viscosity agents, CDRH has concluded that the device is effective in wetting and lubricating silicone acrylate RGP contact lenses.

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VI. Potential Adverse Effects of the Device on Health

Potential adverse effects on health resulting from the use of this device are indicated in the package insert under "ADVERSE REACTIONS" (Attachment B).

VII. Conclusions Drawn From the Studies

The data contained in the PMA provide reasonable assurance that the device is safe and effective for its intended use.

VIII. Panel Recommendation

On June 21, 1988, the Ophthalmic Devices Panel unanimously recommended approval of the PMA subject to the conditions that all administrative requirements be met and that the applicant be in compliance with the device Good Manufacturing Practice (GMP) regulations.

IX. CDRH Decision

After the applicant met the conditions recommended by the Panel, CDRH concluded that the data contained in the PMA provides reasonable assurance that the device is safe and effective for lubricating and wetting silicone acrylate rigid gas permeable contact lenses. Based upon this conclusion, upon information in the PMA and upon review of the labeling, CDRH concurred with the Panel recommendation and approved the application and draft final labeling on MAR 31 1989.

The device shelf-life has been established and approved as 36 months. In an on-site inspection commencing on October 24, 1988, the manufacturing facilities were found to be in compliance with the device GMP regulations.

X. Conditions of Approval

CDRH has determined that the only conditions pertaining to this device are those described in the "Conditions of Approval" enclosed with the approval order. A copy of the package insert is included (Attachment B). All approved labeling is available to interested persons for inspection at:

Food and Drug Administration
Center for Devices and
Radiological Health
PMA Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Spring, Maryland 20910

Attachments A and B

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QUANTIFICATION OF SLIT LAMP OBSERVATIONS

The following classifications are to be used in reporting slit lamp examination findings:

EDEMA	GRADE CLASSIFICATION	STAINING	GRADE CLASSIFICATION
A. None	0	A. None	0
B. Micro-edema — intercellular accumulation of fluid which is limited to the epithelium and is seen only by the use of the slit lamp.		B. Minimal, variable, peripheral stippling.	1
1. Slight amounts in the epithelium, seen only by retro-illumination:		C. Superficial punctate staining, restricted to a peripheral location and consistent in location from examination to examination.	2
(a) Localized — over less than 50% of the cornea.	1	D. Superficial punctate staining, centrally located.	3
(b) Generalized — over more than 50% of the cornea.	2	E. Diffuse superficial punctate staining.	4
2. Moderate amounts in the epithelium, seen by direct illumination:		F. Epithelial dimpling associated with gas bubbles under the contact lens.	5
(a) Localized — over less than 50% of the cornea.	3	G. Branching furrows on the epithelial surface (observed best by use of the cobalt filter and fluorescein).	6
(b) Generalized — over more than 50% of the cornea.	4	H. Abrasions of the epithelium. Note if apparently caused by insertion or removal.	7
C. Gross edema — intracellular cystic accumulation of fluid, viewed by the naked eye using oblique flashlight illumination.		I. Foreign body track staining.	8
1. Slight case, without any stromal involvement.		J. Deep corneal abrasions, ulcerations, permanent scars or other severe complications (explain).	9
(a) Circumscribed — over less than 50% of the cornea.	5		
(b) Generalized — over more than 50% of the cornea.	6		
2. Severe case, with stromal involvement.			
(a) Circumscribed — over less than 50% of the cornea.	7		
(b) Generalized — over more than 50% of the cornea.	8		
VASCULARIZATION		INJECTION	
A. None	0	A. None	0
B. Extension of the limbal vessels more than 1.5 mm. inside limbus.		B. Mild congestion and dilation of the limbal vessels which was not characteristic of the pre-fitting condition (within 1.0 mm. of limbus).	1
1. Lower limbal area only.	1	C. Severe congestion and dilation of the normal limbal vessels.	2
2. Upper limbal area only.	2	D. Conjunctival hyperemia due to excess lacrimation and epiphora.	3
3. Over the entire periphery.	3		
4. Severe (to within 1 mm. of corneal apex) extensions of the limbal vessels into the clear epithelial tissue of the cornea.	4		
5. Other (explain).	5		
IRITIS		OTHER COMPLICATIONS	
A. No flare or cells	0	A. None	0
B. Minimal flare (1+)	1	B. Adnexal changes or changes in the lacrimal or appendages of the eye.	
C. Mild (2+)	2	1. Increase in mucous secretion in the tear fluid.	1
D. Moderate (3+)	3	2. Follicular hypertrophy of the lymphoid follicles of the tarsal conjunctiva.	2
E. Severe (cells & flare) (4+)	4	3. Traumatic iritis.	3
		4. Descemet's membrane wrinkling.	4
		5. Permanent damage caused by opacity or scarring of the cornea (may or may not impair vision).	5
		C. Other (explain).	6

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Please read carefully and keep this package insert for future use in case you have a problem.

SHERMAN LABORATORIES, INC.

STAY-WET 3 is a sterile preserved wetting and "in eye" lubricating solution and rewetting drop for use with silicone acrylate rigid gas permeable (RGP) contact lenses as recommended by the eye care practitioner.

NOTE: STAY-WET 3 does not contain CHLORHEXIDINE or THIMEROSAL

DESCRIPTION:

STAY-WET 3 is a sterile solution containing sodium and potassium chloride salts, polyvinyl pyrrolidone, polyvinyl alcohol, hydroxyethylcellulose sodium bisulfite 0.02%, and preserved with benzyl alcohol 0.1%, sorbic acid 0.05%, and edetate disodium 0.1%.

ACTIONS:

STAY-WET 3 wets lenses prior to insertion and helps remove irritating particles, and moistens lenses to relieve occasional dryness or discomfort.

INDICATIONS:

STAY-WET 3 is indicated for use to wet lenses prior to insertion and to lubricate lenses while they are on the eye.

CONTRAINDICATIONS:

Please note carefully the ingredients as listed. If you are allergic to sodium bisulfite or any other ingredient in STAY-WET 3, do not use this product.

WARNINGS:

* Contains sodium bisulfite, a sulfite that may cause serious allergic-type reactions (e.g., hives, itching, wheezing, anaphylaxis) in certain susceptible persons. Although the overall incidence of sulfite sensitivity in the general population is probably low, it is seen more frequently in asthmatics or in atopic nonasthmatic persons.

* Lens care procedures as recommended by your eye care practitioner must be followed. Failure to follow these procedures may result in serious eye infections. If any unexplained eye discomfort, watering, vision change or redness of the eye occurs, immediately consult your eye care practitioner to identify the cause and begin necessary treatment.

* To avoid contamination, do not touch dropper tip to any surface.

* Close cap tightly after each use.

* If you are allergic to sodium bisulfite or any other ingredient in STAY-WET 3, do not use this product.

PRECAUTIONS:

- * Always wash and rinse hands before handling your lenses.
- * After inserting your lenses, always empty your lens storage case, rinse, and allow to air dry.
- * Store at room temperature 15 - 30° C (59 - 86° F).
- * Keep out of reach of children.
- * Use before expiration date stamped on carton and bottle label.
- * 'STAY-WET 3® is not for use with soft (hydrophilic) contact lenses.

ADVERSE REACTIONS (PROBLEMS AND WHAT TO DO):

The following problems may occur while wearing contact lenses:

- * Redness of the eye
- * Eyes stinging, burning, or itching
- * Excessive watering (tearing) of the eyes
- * Unusual eye secretions
- * Reduced sharpness of vision (visual acuity)
- * Blurred vision
- * Sensitivity to light (photophobia)
- * Dry eyes

If you notice any of the above problems, IMMEDIATELY remove and examine your lenses. If the problem stops, and the lens appears to be undamaged, thoroughly clean, rinse and disinfect the lenses and reinsert them. If the problem continues, or a lens appears to be damaged, IMMEDIATELY remove your lenses and consult your eye care practitioner. DO NOT reinsert a damaged lens.

If any of the above problems occur, a serious condition such as infection, corneal ulcer, neovascularization, or iritis may be present. Seek immediate professional identification and treatment of the problem to avoid serious eye damage. See your Instructions for Wearers Booklet for more information.

DIRECTIONS FOR USE:

General

- * Always wash and rinse your hands before handling your contact lenses.
- * Clean and rinse one lens, the right or left, first (always the same lens first to avoid mix-ups) your right lens first.

WETTING:

- * Remove the lens from the lens storage case and rinse thoroughly as directed by your eye care practitioner. It is important that this rinsing procedure is thorough. The lens should feel squeaky-clean between your fingers. If not, re-rinse the lens. All disinfecting and storage solution MUST be removed from the lens before wetting with STAY-WET 3 and inserting the lens.
- * Apply 2 drops of STAY-WET 3 over all surfaces of the lens WITHOUT rubbing the lens.
- * Insert the lens as instructed by your eye care practitioner.
- * Repeat the procedure with the other lens.
- * Empty your lens storage case, rinse under running hot tap water, and allow to air dry.

REV 3/14/89

Lubricating

When your lenses feel dry apply no more than two (2) drops of STAY-WET 3® directly in the eye.

HOW SUPPLIED:

STAY-WET 3® is supplied sterile in 1 fl. oz. (30 mL) plastic bottles. Bottles and cartons are marked with lot numbers and expiration date.

EACH CONTAINER IS TAMPER-EVIDENT SEALED. IF THE SEAL AROUND THE BOTTLE CAP IS MISSING OR BROKEN, DO NOT USE THIS PRODUCT.

SHERMAN LABORATORIES, INC.
ABITA SPRINGS, LA 70420

Printed (Mo/Yr)

REV 3/14/89

THE FOLLOWING IS A MOCK UP OF THE INSERT FOR THE LOBOB EQUIVALENT OF STAY-WET 3, LOBOB W/RW. EXCEPT FOR LOBOB TRADE NAME

Please read carefully and keep this package insert for future use in case you have a problem.

LOBOB LABORATORIES, INC.

Drop

LOBOB W/RW ~~Solution~~ is a sterile preserved wetting and "in-eye" lubricating solution and rewetting drop for use with fluoro/silicone acrylate and silicone acrylate rigid gas permeable (RGP) contact lenses as recommended by the eye care practitioner.

Drop

NOTE: LOBOB W/RW ~~Solution~~ does not contain CHLORHEXIDINE or THIMEROSAL.

DESCRIPTION: *Drop*

LOBOB W/RW ~~Solution~~ is a sterile solution containing sodium and potassium chloride salts, polyvinyl pyrrolidone, polyvinyl alcohol, hydroxyethylcellulose, sodium bisulfite 0.02%, and preserved with benzyl alcohol 0.1%, sorbic acid 0.05%, and ~~trisodium~~ *disodium* edetate 0.1%.

ACTIONS: LOBOB W/RW ~~Solution~~ wets lenses prior to insertion and helps remove irritating particles, and moistens lenses to relieve occasional dryness or discomfort.

INDICATIONS: LOBOB W/RW ~~Solution~~ *Drop* is indicated for use to wet lenses prior to insertion and to lubricate lenses while they are on the eye.

and silicone acrylate rigid gas permeable contact

fluoro-silicone acrylate

CONTRAINDICATION: Please note carefully the ingredients as listed. If you are allergic to sodium bisulfite or any other ingredient in LOBOB W/RW ~~Solution~~, do not use this product.

WARNINGS:

- .Contains sodium bisulfite, a sulfite that may cause serious allergic-type reactions (e.g., hives, itching, wheezing, anaphylaxis) in certain susceptible persons. Although the overall incidence of sulfite sensitivity in the general population is probably low, it is seen more frequently in asthmatics or in atopic nonasthmatic persons.
- .Lens care procedures as recommended by your eye care practitioner must be followed. Failure to follow these procedures may result in serious eye infections. If any unexplained eye discomfort, watering, vision change or redness of the eye occurs, immediately remove your lenses and consult your eye care practitioner to identify the cause and begin necessary treatment.
- .To avoid contamination, do not touch dropper tip to any surface.
- .Close cap tightly after each use.
- .If you are allergic to sodium bisulfite or any other ingredient in LOBOB W/RW Solution, do not use this product.

PRECAUTIONS:

- .Always wash and rinse hands before handling your lenses.
- .After inserting your lenses, always empty your lens storage case, rinse and allow to air dry.
- .Store at room temperature 15-30°C (59-86°F)
- .Keep out of reach of children.
- .Use before the expiration date stamped on carton & bottle label.
- .LOBOB W/RW ~~Solution~~^{Drop} is not for use with soft (hydrophilic) contact lenses.

ADVERSE REACTIONS (PROBLEMS AND WHAT TO DO):

The following problems may occur while wearing contact lenses:

- .Redness of the eye
- .Eyes stinging, burning, or itching
- .Excessive watering (tearing) of the eyes
- .Unusual eye secretions
- .Reduced sharpness of vision (visual acuity)
- .Blurred vision
- .Sensitivity to light (photophobia)
- .Dry eyes

If you notice any of the above problems, IMMEDIATELY remove and examine your lenses. If the problem stops, and the lenses appear to be undamaged, thoroughly clean, rinse, and disinfect the lenses and reinsert them. If the problem continues, or a lens appears to be damaged, IMMEDIATELY remove your lenses and consult your eye care practitioner. DO NOT reinsert a damaged lens. If any of the above problems occur, a serious condition such as infection, corneal ulcer, neovascularization, or iritis may be present. Seek immediate professional identification and treatment of the problem to avoid serious eye damage. See your Instructions for Wearers Booklet for more information.

DIRECTIONS FOR USE:

General

- .Always wash and rinse your hands before handling your contact lenses.
- .Clean and rinse one lens, the right or left, first (always the same lens first to avoid mix-ups)

WETTING:

- .Remove the lens from the lens storage case and rinse thoroughly as directed by your eye care practitioner. It is important that this rinsing procedure is thorough. The lens should feel squeaky-clean between your fingers. If not, re-rinse the lens. All disinfecting and storage solution MUST be removed from the lens before wetting with LOBOB W/RW Solution and inserting the lens. ^{Drop}
- .Apply two drops of LOBOB W/RW ~~Solution~~^{Drop} over all surfaces of the lens WITHOUT rubbing the lens.
- .Insert the lens as instructed by your eye care practitioner.
- .Repeat the procedure with the other lens.
- .Empty your lens storage case, rinse under running hot tap

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Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Mr. Daniel J. Manelli
Consultant for Lobob Laboratories, Inc.
Farkas & Manelli, P.L.L.C.
2000 M Street N.W.
Suite 700
Washington, DC 20036-3307

APR 30 1998

Re: P940025
Lobob W/RW Drop
Filed: May 23, 1995
Amended: May 25, June 9, July 17, and August 2, 1995; and
March 26, May 7, November 5 and 15, 1996; and April 21, 1998

Dear Mr. Manelli:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of the premarket approval application (PMA) that you submitted on behalf of Lobob Laboratories, Inc., for the Lobob W/RW Drop. This device is indicated for use to wet fluoro-silicone acrylate and silicone acrylate rigid gas permeable contact lenses prior to insertion and to lubricate lenses while they are on the eye. Your client may begin commercial distribution of the device upon receipt of this letter.

Expiration dating for this device has been established and approved at 18 months for the 1 fl. oz. (30 ml) and 12 months for the 0.3 fl. oz. (10 ml) bottle sizes. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(8).

CDRH will notify the public of its decision to approve the PMA by making available a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/cdrh/pmapage.html>. Written requests for this information can also be made to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., Rm. 1-23, Rockville, MD 20857. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Effective July 7, 1997, CDRH reclassified contact lens care products from class III (premarket approval) to class II (special controls). Although the device is subject to the reclassification order, CDRH continued to process this application as a PMA to facilitate approval since the only outstanding issue at the time of reclassification was compliance with the Good Manufacturing Practice Regulation. This issue was subsequently resolved on April 30, 1998.

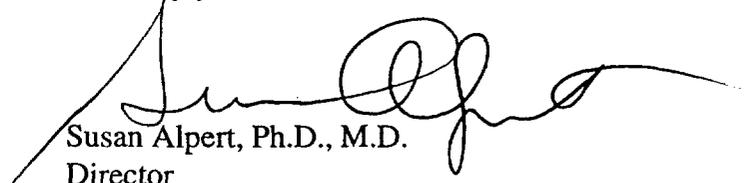
Future modifications of the device are subject to the premarket notification (510(k)) provisions of the act. Guidance for preparing a 510(k) submission is found in the "Guidance for Industry, Premarket Notification (510(k)) Guidance Document for Contact Lens Care Products" dated May 1, 1997, which can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/cdrh>. You may obtain a hard copy of the guidance by faxing your request to the Division of Small Manufacturers Assistance [fax (301) 443-8818].

All correspondence regarding 510(k) submission should be submitted to the address below:

510(k) Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Ms. Muriel Gelles or James F. Saviola, O.D., at (301) 594-1744, or Kathy Poneleit at (301) 594-2186.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Susan Alpert", with a long horizontal flourish extending to the right.

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Summary of Safety and Effectiveness Data

I. General Information

- A. Device Generic Name: sterile lubricating and wetting solution for use with fluoro-silicone acrylate and silicone acrylate rigid gas permeable contact lenses
- B. Device Trade Name: Lobob W/RW Drop
- C. Applicant's Name and Address: Mr. Daniel J. Manelli
Consultant
Lobob Laboratories, Inc.
1440 Atteberry Lane
San Jose, CA 95131
- D. Premarket Approval Application (PMA) Number: P940025
- E. Date of Notice of Approval to Applicant: APR 30 1998

II. Indications

Lobob W/RW Drop is indicated for use to wet fluoro-silicone acrylate and silicone acrylate rigid gas permeable contact lenses prior to insertion and to lubricate lenses while they are on the eye.

III. Device Description

Lobob W/RW Drop is a sterile solution containing sodium and potassium chloride salts, polyvinyl pyrrolidone, polyvinyl alcohol, hydroxyethylcellulose, sodium bisulfite 0.02%, and preserved with benzyl alcohol 0.1%, sorbic acid 0.05%, and edetate disodium 0.1%.

IV. Center for Devices and Radiological Health (CDRH) Decision

The application includes by reference the data in P870029 for STAY-WET 3^R and all related supplements that led to the approval of STAY-WET 3^R, submitted by Sherman Laboratories, Inc. and approved by FDA on March 31, 1989. Sherman Laboratories, Inc. has authorized Lobob Laboratories, Inc. to incorporate by reference the information contained in its approved PMA to manufacture the device.

CDRH approval of Lobob Laboratories, Inc.'s PMA is based on (1) the safety and effectiveness data contained in PMA P870029 and related supplements and (2) the results of the FDA inspections of the manufacturing facilities. A summary of safety and effectiveness data for the STAY-WET 3^R appears in Attachment A.

Effective July 7, 1997, CDRH reclassified contact lens care products from class III (premarket approval) to class II (special controls). Although the device is subject to the reclassification order, CDRH continued to process this application as a PMA to facilitate approval since the only outstanding issue at the time of reclassification was compliance with the Good Manufacturing Practice Regulation. This issue was subsequently resolved on APR 30 1998.

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices Panel for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel. CDRH approved this application and final labeling on APR 30 1998.

The device shelf-life has been established and approved as 18 months.

V. Potential Adverse Effects of the Device on Health

Potential adverse effects on health resulting from the use of this device are listed in the package insert under "ADVERSE REACTIONS (PROBLEMS AND WHAT TO DO)" (Attachment B).

VI. Conditions of Approval

CDRH has determined that no special restrictions or conditions pertain other than those described in the "Conditions of Approval" enclosed with the approval order. A copy of the approved draft labeling is attached (Attachment B).

Attachments A and B

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Summary of Safety and Effectiveness Data

I. General Information

- A. Device Generic Name: sterile lubricating and wetting solution for use with silicone acrylate rigid gas permeable contact lenses
- B. Device Trade Name: STAY-WET 3®
- C. Applicant's Name and Address: Sherman Laboratories, Inc.
P.O. Box 368
Abita Springs, Louisiana 70420
- D. Premarket Approval Application (PMA) Number: P870029
- E. Date of Panel Recommendation: June 21, 1988
- F. Date of Notice of Approval to Applicant: MAR 31 1989

II. Indications

STAY-WET 3® is indicated for use to wet silicone acrylate rigid gas permeable (RGP) contact lenses prior to insertion and to lubricate lenses while they are on the eye.

III. Device Description

STAY-WET 3® is a sterile solution containing sodium chloride, potassium chloride, polyvinyl pyrrolidone (PVP), polyvinyl alcohol (PVA), hydroxyethylcellulose and sodium bisulfite 0.02%, preserved with benzyl alcohol 0.1%, sorbic acid 0.05% and edetate disodium 0.1%.

IV. Alternative Practices or Procedures

Alternative practices or procedures available to the patient are the use of other commercially available solutions for the same indications.

V. Summary of Studies

A. Preclinical:

1. Toxicology: The applicant conducted the battery of tests outlined in "Toxicology Guidelines" section of the Class III Contact Lens Product Guideline, an FDA guideline dated May 1983. In addition to the guideline testing, the applicant provided the following toxicology information for the preservative, benzyl alcohol:

S

- a. guinea pig maximization test was conducted to assess the sensitization potential of benzyl alcohol
- b. Cochet-Bonett Test was conducted on humans to determine the possible anaesthetic effect of benzyl alcohol to the cornea
- c. corneal penetration test was conducted in rabbits to determine the adsorption and distribution in ocular tissue and to determine if benzyl alcohol is metabolized during corneal penetration
- d. corneal epithelial wound healing study was conducted in rabbits to determine if benzyl alcohol had any effect on the rate of epithelial wound healing
- e. Product Safety Information Sheet containing the following information:
 1. the acute oral LD50 is 1230 mg/kg to 3100 mg/kg in rats
 2. the acute oral LD50 is 1580 mg/kg in mice
 3. the acute oral LD50 is 1040 mg/kg in rabbits
 4. the acute dermal LD50 is 2000 mg/kg in rabbits
 5. the acute inhalation LC50 is 1000 ppm in rats after an 8-hour inhalation exposure
 6. benzyl alcohol meets the requirements of the Federal OSHA Hazard Communication Standard (29 CFR 1900.1200)

Conclusion:

The results from the guideline testing for the device along with the additional testing described above provide reasonable assurance that the solution and its preservatives, benzyl alcohol, at the concentration proposed for use (0.1%), and sorbic acid, raise no acute toxicological concerns and support the safety of the device for its intended use as stated in the approved labeling. The safety of sodium bisulfite has been established as safe for use in ophthalmic solutions as listed in the OTC ophthalmic monograph. The labeling contains adequate warning regarding the use of the product by persons with sensitivities to the ingredient such as asthmatics and contraindicates use of the device by persons allergic to any ingredients in the solution with special emphasis placed on asthmatic persons.

2. Microbiology: The applicant conducted the battery of tests outlined in "Microbiology Guidelines" section of the Class III Contact Lens Product Guideline, an FDA guideline dated May 1983.

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Conclusion:

The results from these tests provide reasonable assurance that the solution remains sterile as packaged for at least 36 months.

3. Lens/Solution Compatibility: The applicant conducted tests to establish that the solution does not adversely affect lens color, base curve, diameter, center thickness, and power. In these tests, 5 Polycon, 5 Polycon II, 1 Boston IV, 4 Paraperm O₂ Plus, and 5 Optacryl K lenses were cycled through 30 cleaning and disinfection cycles. The lenses were then examined to determine the effect of the test solution on the lenses. There were no changes in lens color and parameters.

Conclusion:

The results from these tests provide reasonable assurance that the solution is compatible with clear and tinted silicone acrylate rigid gas permeable contact lenses.

4. Solution Stability: The applicant conducted tests to establish the stability of the solution and the appropriate expiration dating. The test solution was packaged into the finished product containers stored at various temperatures, and examined for conformance to original specifications.

Conclusion:

The results from these tests provide reasonable assurance that the solution remains stable as packaged for at least 36 months in its 1 fl. oz. (30 mL) container.

5. Preservative Uptake/Release: A preservative uptake/release study was conducted by the applicant for benzyl alcohol and sorbic acid. Two lenses each of Polycon, Polycon II, Boston II, Paraperm O₂ Plus, and Optacryl K silicone acrylate rigid gas permeable contact lenses were soaked in the solution, and the uptake and release of benzyl alcohol and sorbic acid was measured in accordance with the FDA Guidelines dated May 1983.

Conclusion:

The results from these tests demonstrate minimal risk to patients from uptake and release of the preservatives by silicone acrylate rigid gas permeable contact lenses and supports the safety of the device for its intended use when accompanied by appropriate labeling. The labeling for the device contraindicates use of the device by persons allergic to any ingredients in the solution. In addition, the labeling for the device warns that the solution is not to be used directly in the eye.

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6. **Wetting Effectiveness:** The applicant conducted an in vitro contact angle study to assess the effectiveness of Stay Wet 3[®] in the wetting of silicone acrylate RGP lenses. Using 1 each of Boston II, Paraperm O₂ Plus and Polycon II silicone acrylate lenses, contact angle measurements were taken using the Captive Bubble method. Lenses were treated with Stay Wet 3[®], submerged in saline solution at 25° C, and suspended with the front curve down. A bubble of air was released below the lens and trapped on the front curve. The angle of contact between the bubble and the lens surface was measured in degrees using a Gonimeter. Initially after treatment with Stay Wet 3[®] (zero time), the lenses were very wettable and the bubble would not adhere to the lens surface. Measurements could only be performed on the treated lenses after 5 minutes equilibration time in the saline; therefore, the 5 minute time was used as the baseline measurement. Measurements were also provided at the 15 minute and 30 minute intervals to determine if the wettability effect would last for a sustained period of time; i.e., at least 30 minutes. Results were as follows:

Contact Angle by Time Measured in Degrees

<u>Lens</u>	<u>5 minutes</u>	<u>15 minutes</u>	<u>30 minutes</u>
Boston II	19	20	21
Paraperm O ₂ Plus	20	20	22
Polycon II	19	21	22

Conclusion:

The results from this study indicate that the wettability effect of the device as determined by the contact angle measurements was immediate and remained essentially unchanged for at least 30 minutes when compared to baseline measurements (5 minutes). The results provide supporting evidence that the device is effective in wetting silicone acrylate RGP lenses.

7. **Additional Information:** The applicant offered additional information to provide support of the effectiveness of the preservative, benzyl alcohol. This information includes references to USP XXI (page 1195) which lists benzyl alcohol as one of the commonly used antimicrobial agents and to United States Dispensatory, 26th Edition, (page 198) which lists benzyl alcohol as having bacteriostatic effects.

Conclusion:

The information cited above provides additional supportative evidence of the effectiveness of benzyl alcohol as an antimicrobial agent.

B. **Clinical:**

The purpose of the clinical study was to evaluate the safety and effectiveness of the device in accordance with the proposed labeling.

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The clinical study was conducted in accordance with the "Clinical Guidelines" section of the Class III Contact lens Product Guidelines, an FDA guideline dated May 1983.

Patient Selection Criteria

The patients enrolled into this clinical study were to meet the following criteria:

1. be willing to adhere to the regimen of hygiene prescribed;
2. have normal eyes as defined in the protocol and use no ocular medications; and
3. have need of an optical correction.

Study Population

A total of 228 patients (451 eyes) was enrolled by 9 investigators into this clinical study. There were 148 females and 80 males ranging in age from 7 years to 73 years. Of the 228 patients (451 eyes) enrolled into the study, 213 patients (423 eyes) completed the 6-month study, and 15 patients (28 eyes) were discontinued from the study as discussed on page 9 of this summary. All patients in the study used STAY-WET 3® and de-STAT 3® (a cleaning, storage and conditioning solution which is the subject of another PMA). Lenses worn during the study were:

<u>Lenses</u>	<u>No. of Eyes</u>
Optacryl and Optacryl K	126
Boston II	124
Paraperm	57
Polycon and Polycon II	50
Silcon	44
Optacryl 60	32
Ultraflex	4
Flex	4
Airlens	2
B.P. Flex	2
Bioflex	2
GP II Hydrocurve	2
Ellipsecon	2

Study Period

The clinical study began on March 8, 1984, and ended on April 16, 1985. The study period was 6 months.

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Findings

1. Safety:

Adverse Reactions

In evaluating this device, an adverse reaction was considered to be a serious, vision-threatening problem that was unanticipated, but which might have been attributed to the use of the study device. There were no adverse reactions reported during the course of this clinical study.

Slit Lamp Findings

A positive slit lamp finding is considered to be a routinely occurring complication that would be expected with or without the presence of contact lenses and with or without the use of the study device. The degree of severity can range from very slight to serious. At the least severe, the findings present no medical concerns and are noticeable only by microscopic slit lamp examination. In a severe state, the findings require medical treatment.

Slit lamp examinations were performed initially and periodically throughout the study. The applicant used the classification of slit lamp findings as outlined in attachment A. Positive slit lamp findings for the 423 eyes completing the study were as follows:

<u>Slit Lamp Finding</u>	<u>Initial Visit 423 eyes</u>	<u>Follow-up Visits 2,526 eyes</u>	<u>Final Visit 423 eyes</u>
Edema			
Grade 1	0	1	0
Injection			
Grade 1	0	7	0
Staining			
Grade 1	2	49	9
Grade 2	0	4	0
Grade 3	2	2	0
Grade 4	0	5	0
Grade 5	0	1	1
Grade 8	0	1	1
Iritis	0	0	0
Vascular- ization			
Grade 1	0	4	0
Other	0	0	0

One patient had recurrent grade 3 staining in both eyes at the initial and 2-week visits. The condition resolved as the study progressed.

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There were 5 reports of grade 4 staining (diffuse superficial punctate staining), 2 reports of grade 5 staining (epithelial dimpling associated with gas bubbles under the lens), and 2 reports of grade 8 staining (foreign body track staining) during the study. In each case the findings resolved with no sequelae, and all patients successfully completed the study.

Conclusion:

There were no positive slit lamp findings requiring medical treatment during this study. The positive slit lamp findings in this clinical study are within expected limits for contact lens wear and do not raise any significant concerns regarding the safety of the device when used as directed in the approved labeling.

Patient Symptoms, Problems and Complaints

Patient symptoms, problems and complaints were reported by the investigators during the clinical study. Of the 3,872 eye examinations conducted, a total of 2,971 eye examination reports were provided for patient symptoms, problems and complaints during the course of the 6-month study. Patient symptoms, problems and complaints (multiple reports) were reported as follows:

	<u>No. Reports</u> <u>All Visits</u>
Awareness of lens	13
Excessive blink rate	8
Variable vision	8
Lenses need cleaning	8
Pain, burning, itching	5
Excessive movement	5
Spectacle blur	4
Handling problems	4
Reading problems	4
Flare	3
Excessive tearing	3
Distance vision blurred	2
Eyes clouded up	2
Dry eyes	2
Scratching	2
Tired eyes	2
Eyes feel swollen	2
Discomfort	1
Excessive blink rate and movement	1

Conclusion:

The patient symptoms, problems and complaints reported during this study were within expected limits for contact lens wear and do not raise any significant concerns about the safety or effectiveness of the device.

2. Effectiveness:

Visual Acuity

For the 423 eyes completing the study, visual acuity with lenses was reported as 20/30 or better for 407 of 415 eyes at the initial visit and 419 of the 421 eyes at the final visit. Visual acuity was not reported for 8 eyes at the initial visit and 2 eyes at the final visit. Visual acuity data was provided for the initial visit and was compared to visual acuity at the last visit. Results for the completer eyes were:

<u>Visual Acuity</u>	<u>Initial Visit (423 eyes)</u>	<u>Final Visit (423 eyes)</u>
20/20 or better	372	405
20/25	26	14
20/30	9	0
20/40	6	0
20/50	0	0
20/60	1	1
20/150	0	1
20/200	1	0
Not reported	8	2

Conclusion:

There were no decreases in visual acuity greater than 1 Snellen line. A fluctuation in visual acuity of 1 Snellen line is not unusual for a contact lens and contact lens solution study due to measuring techniques and normal fluctuation and is not significant in terms of visual acuity. The visual acuity results in this clinical study do not raise any significant concerns regarding the safety and effectiveness of the device and provide reasonable assurance that the device does not adversely affect the lenses.

Lens Wearing Time

The average daily lens wearing time ranged from 14 hours at the 2-week visit to 15.3 hours at the final visit.

Conclusion:

The lens wearing times reported for this study provide reasonable assurance that most patients were wearing their lenses for at least 14 hours each day without negative effects from the use of the device.

Discontinued Patients

There were 15 patients (28 eyes) discontinued from this study. Reasons for discontinuation were:

<u>Reason</u>	<u>No. Eyes</u>
Lost-to-follow-up	20
Moved	4
Discomfort	2
Failure to comply with instructions	2

There were no eyes discontinued for reason of pathology. All eyes discontinued from the study were discontinued by the 8-week visit.

Conclusion:

The reasons for and incidence of discontinuance in this clinical study are within expected limits for contact lens wear and do not raise any significant concerns regarding the safety and effectiveness of the device.

Lens Replacements

There were 34 lenses replaced during this clinical study. Reasons reported for replacements were as follows:

<u>Reason</u>	<u>No. of Lenses</u>
Acuity	11
Back-up lenses	10
Lost	4
Spectacle blur	2
Physiology and fitting	2
Not specified	2
Comfort	1
Fitting	1
Warpage	1

"Physiology and fitting" was reported as grade 1 edema and lens parameter change.

Conclusion:

The reasons for lens replacements in this study are within expected limits for contact lens wear. These reasons and numbers of replacements do not raise any significant concerns about the safety and effectiveness of the device.

Wetting and Lubricating Evaluation

At the 6-month visit the 213 patients completing the study were asked to evaluate the subject device. Vision was reported as very good by 205 patients and acceptable for 8 patients; comfort was very good for 206 patients and acceptable for 7 patients; and physiology response (slit lamp findings) was reported as very good for 206 patients and acceptable for 7 patients.

Of these 213 patients 155 patients experienced improved wetting of their lenses compared to the wetting solution previously used and 149 patients indicated that the subject device was less irritating than their previous lubricating solution.

One year after completion of the study patients were asked to evaluate the subject device. Of the 213 patients completing the study, responses were received from 164 patients. Of these, 155 patients reported that lens wetting was improved, 149 patients reported that the subject device was less irritating than their previous lubricating and wetting solution, and 156 patients were more satisfied with the subject device than with their previous lubricating and wetting solution.

All patients completing the study used the subject device as directed prior to lens insertion. The device was used as a lubricating and rewetting solution twice each day for 26 patients and once each day for 70 patients. Because patients were instructed to use the device for lubricating and rewetting as needed the solution was not used as a lubricant by 69 patients that did not experience dry eyes. Use of the solution was not reported for 48 patients. However, the absence of adverse reactions and the relatively low reports of positive slit lamp findings indicates there were no negative reports by these 48 patients.

Conclusion:

Based upon the clinical experineces cited above and the ingredients of the device which are listed in the OTC monograph as viscosity agents, CDRH has concluded that the device is effective in wetting and lubricating silicone acrylate RGP contact lenses.

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VI. Potential Adverse Effects of the Device on Health

Potential adverse effects on health resulting from the use of this device are indicated in the package insert under "ADVERSE REACTIONS" (Attachment B).

VII. Conclusions Drawn From the Studies

The data contained in the PMA provide reasonable assurance that the device is safe and effective for its intended use.

VIII. Panel Recommendation

On June 21, 1988, the Ophthalmic Devices Panel unanimously recommended approval of the PMA subject to the conditions that all administrative requirements be met and that the applicant be in compliance with the device Good Manufacturing Practice (GMP) regulations.

IX. CDRH Decision

After the applicant met the conditions recommended by the Panel, CDRH concluded that the data contained in the PMA provides reasonable assurance that the device is safe and effective for lubricating and wetting silicone acrylate rigid gas permeable contact lenses. Based upon this conclusion, upon information in the PMA and upon review of the labeling, CDRH concurred with the Panel recommendation and approved the application and draft final labeling on MAR 31 1989.

The device shelf-life has been established and approved as 36 months. In an on-site inspection commencing on October 24, 1988, the manufacturing facilities were found to be in compliance with the device GMP regulations.

X. Conditions of Approval

CDRH has determined that the only conditions pertaining to this device are those described in the "Conditions of Approval" enclosed with the approval order. A copy of the package insert is included (Attachment B). All approved labeling is available to interested persons for inspection at:

Food and Drug Administration
Center for Devices and
Radiological Health
PMA Document Mail Center (HFZ-401)
8757 Georgia Avenue
Silver Spring, Maryland 20910

Attachments A and B

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QUANTIFICATION OF SLIT LAMP OBSERVATIONS

The following classifications are to be used in reporting slit lamp examination findings:

EDEMA	GRADE CLASSIFICATION	STAINING	GRADE CLASSIFICATION
A. None	0	A. None	0
B. Micro-edema — intercellular accumulation of fluid which is limited to the epithelium and is seen only by the use of the slit lamp.		B. Minimal, variable, peripheral stippling.	1
1. Slight amounts in the epithelium, seen only by retro-illumination:		C. Superficial punctate staining, restricted to a peripheral location and consistent in location from examination to examination.	2
(a) Localized — over less than 50% of the cornea.	1	D. Superficial punctate staining, centrally located.	3
(b) Generalized — over more than 50% of the cornea.	2	E. Diffuse superficial punctate staining.	4
2. Moderate amounts in the epithelium, seen by direct illumination:		F. Epithelial dimpling associated with gas bubbles under the contact lens.	5
(a) Localized — over less than 50% of the cornea.	3	G. Branching furrows on the epithelial surface (observed best by use of the cobalt filter and fluorescein).	6
(b) Generalized — over more than 50% of the cornea.	4	H. Abrasions of the epithelium. Note if apparently caused by insertion or removal.	7
C. Gross edema — intracellular cystic accumulation of fluid, viewed by the naked eye using oblique flashlight illumination.		I. Foreign body track staining.	8
1. Slight case, without any stromal involvement.		J. Deep corneal abrasions, ulcerations, permanent scars or other severe complications (explain).	9
(a) Circumscribed — over less than 50% of the cornea.	5		
(b) Generalized — over more than 50% of the cornea.	6		
2. Severe case, with stromal involvement.			
(a) Circumscribed — over less than 50% of the cornea.	7		
(b) Generalized — over more than 50% of the cornea.	8		
VASCULARIZATION		INJECTION	
A. None	0	A. None	0
B. Extension of the limbal vessels more than 1.5 mm. inside limbus.		B. Mild congestion and dilation of the limbal vessels which was not characteristic of the pre-fitting condition (within 1.0 mm. of limbus).	1
1. Lower limbal area only.	1	C. Severe congestion and dilation of the normal limbal vessels.	2
2. Upper limbal area only.	2	D. Conjunctival hyperemia due to excess lacrimation and epiphora.	3
3. Over the entire periphery.	3		
4. Severe (to within 1 mm. of corneal apex) extensions of the limbal vessels into the clear epithelial tissue of the cornea.	4		
5. Other (explain).	5		
IRITIS		OTHER COMPLICATIONS	
A. No flare or cells	0	A. None	0
B. Minimal flare (1+)	1	B. Adnexal changes or changes in the lacrimal or appendages of the eye.	
C. Mild (2+)	2	1. Increase in mucous secretion in the tear fluid.	1
D. Moderate (3+)	3	2. Follicular hypertrophy of the lymphoid follicles of the tarsal conjunctiva.	2
E. Severe (cells & flare) (4+)	4	3. Traumatic iritis.	3
		4. Descemet's membrane wrinkling.	4
		5. Permanent damage caused by opacity or scarring of the cornea (may or may not impair vision).	5
		C. Other (explain).	6

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Please read carefully and keep this package insert for future use in case you have a problem.

SHERMAN LABORATORIES, INC.

STAY-WET 3 is a sterile preserved wetting and "in eye" lubricating solution and rewetting drop for use with silicone acrylate rigid gas permeable (RGP) contact lenses as recommended by the eye care practitioner.

NOTE: STAY-WET 3 does not contain CHLORHEXIDINE or THIMEROSAL

DESCRIPTION:

STAY-WET 3 is a sterile solution containing sodium and potassium chloride salts, polyvinyl pyrrolidone, polyvinyl alcohol, hydroxyethylcellulose sodium bisulfite 0.02%, and preserved with benzyl alcohol 0.1%, sorbic acid 0.05%, and edetate disodium 0.1%.

ACTIONS:

STAY-WET 3 wets lenses prior to insertion and helps remove irritating particles, and moistens lenses to relieve occasional dryness or discomfort.

INDICATIONS:

STAY-WET 3 is indicated for use to wet lenses prior to insertion and to lubricate lenses while they are on the eye.

CONTRAINDICATIONS:

Please note carefully the ingredients as listed. If you are allergic to sodium bisulfite or any other ingredient in STAY-WET 3, do not use this product.

WARNINGS:

* Contains sodium bisulfite, a sulfite that may cause serious allergic-type reactions (e.g., hives, itching, wheezing, anaphylaxis) in certain susceptible persons. Although the overall incidence of sulfite sensitivity in the general population is probably low, it is seen more frequently in asthmatics or in atopic nonasthmatic persons.

* Lens care procedures as recommended by your eye care practitioner must be followed. Failure to follow these procedures may result in serious eye infections. If any unexplained eye discomfort, watering, vision change or redness of the eye occurs, immediately consult your eye care practitioner to identify the cause and begin necessary treatment.

* To avoid contamination, do not touch dropper tip to any surface.

* Close cap tightly after each use.

* If you are allergic to sodium bisulfite or any other ingredient in STAY-WET 3, do not use this product.

PRECAUTIONS:

- * Always wash and rinse hands before handling your lenses.
- * After inserting your lenses, always empty your lens storage case, rinse, and allow to air dry.
- * Store at room temperature 15 - 30° C (59 - 86° F).
- * Keep out of reach of children.
- * Use before expiration date stamped on carton and bottle label.
- * 'STAY-WET 3® is not for use with soft (hydrophilic) contact lenses.

ADVERSE REACTIONS (PROBLEMS AND WHAT TO DO):

The following problems may occur while wearing contact lenses:

- * Redness of the eye
- * Eyes stinging, burning, or itching
- * Excessive watering (tearing) of the eyes
- * Unusual eye secretions
- * Reduced sharpness of vision (visual acuity)
- * Blurred vision
- * Sensitivity to light (photophobia)
- * Dry eyes

If you notice any of the above problems, IMMEDIATELY remove and examine your lenses. If the problem stops, and the lens appears to be undamaged, thoroughly clean, rinse and disinfect the lenses and reinsert them. If the problem continues, or a lens appears to be damaged, IMMEDIATELY remove your lenses and consult your eye care practitioner. DO NOT reinsert a damaged lens.

If any of the above problems occur, a serious condition such as infection, corneal ulcer, neovascularization, or iritis may be present. Seek immediate professional identification and treatment of the problem to avoid serious eye damage. See your Instructions for Wearers Booklet for more information.

DIRECTIONS FOR USE:

General

- * Always wash and rinse your hands before handling your contact lenses.
- * Clean and rinse one lens, the right or left, first (always the same lens first to avoid mix-ups) your right lens first.

WETTING:

- * Remove the lens from the lens storage case and rinse thoroughly as directed by your eye care practitioner. It is important that this rinsing procedure is thorough. The lens should feel squeaky-clean between your fingers. If not, re-rinse the lens. All disinfecting and storage solution MUST be removed from the lens before wetting with STAY-WET 3 and inserting the lens.
- * Apply 2 drops of STAY-WET 3 over all surfaces of the lens WITHOUT rubbing the lens.
- * Insert the lens as instructed by your eye care practitioner.
- * Repeat the procedure with the other lens.
- * Empty your lens storage case, rinse under running hot tap water, and allow to air dry.

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Lubricating

When your lenses feel dry apply no more than two (2) drops of STAY-WET 3® directly in the eye.

HOW SUPPLIED:

STAY-WET 3® is supplied sterile in 1 fl. oz. (30 mL) plastic bottles. Bottles and cartons are marked with lot numbers and expiration date.

EACH CONTAINER IS TAMPER-EVIDENT SEALED. IF THE SEAL AROUND THE BOTTLE CAP IS MISSING OR BROKEN, DO NOT USE THIS PRODUCT.

SHERMAN LABORATORIES, INC.
ABITA SPRINGS, LA 70420

Printed (Mo/Yr)

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THE FOLLOWING IS A MOCK UP OF THE INSERT FOR THE LOBOB EQUIVALENT OF STAY-WET 3, LOBOB W/RW. EXCEPT FOR LOBOB TRADE NAME

Please read carefully and keep this package insert for future use in case you have a problem.

LOBOB LABORATORIES, INC.

Drop

LOBOB W/RW ~~Solution~~ is a sterile preserved wetting and "in-eye" lubricating solution and rewetting drop for use with fluoro/silicone acrylate and silicone acrylate rigid gas permeable (RGP) contact lenses as recommended by the eye care practitioner.

Drop

NOTE: LOBOB W/RW ~~Solution~~ does not contain CHLORHEXIDINE or THIMEROSAL.

DESCRIPTION: *Drop*

LOBOB W/RW ~~Solution~~ is a sterile solution containing sodium and potassium chloride salts, polyvinyl pyrrolidone, polyvinyl alcohol, hydroxyethylcellulose, sodium bisulfite 0.02%, and preserved with benzyl alcohol 0.1%, sorbic acid 0.05%, and ~~trisodium~~ *disodium* edetate 0.1%.

ACTIONS: LOBOB W/RW ~~Solution~~ wets lenses prior to insertion and helps remove irritating particles, and moistens lenses to relieve occasional dryness or discomfort.

INDICATIONS: LOBOB W/RW ~~Solution~~ *Drop* is indicated for use to wet lenses prior to insertion and to lubricate lenses while they are on the eye.

and silicone acrylate rigid gas permeable contact

fluoro-silicone acrylate

CONTRAINDICATION: Please note carefully the ingredients as listed. If you are allergic to sodium bisulfite or any other ingredient in LOBOB W/RW ~~Solution~~, do not use this product.

WARNINGS:

- .Contains sodium bisulfite, a sulfite that may cause serious allergic-type reactions (e.g., hives, itching, wheezing, anaphylaxis) in certain susceptible persons. Although the overall incidence of sulfite sensitivity in the general population is probably low, it is seen more frequently in asthmatics or in atopic nonasthmatic persons.
- .Lens care procedures as recommended by your eye care practitioner must be followed. Failure to follow these procedures may result in serious eye infections. If any unexplained eye discomfort, watering, vision change or redness of the eye occurs, immediately remove your lenses and consult your eye care practitioner to identify the cause and begin necessary treatment.
- .To avoid contamination, do not touch dropper tip to any surface.
- .Close cap tightly after each use.
- .If you are allergic to sodium bisulfite or any other ingredient in LOBOB W/RW Solution, do not use this product.

PRECAUTIONS:

- .Always wash and rinse hands before handling your lenses.
- .After inserting your lenses, always empty your lens storage case, rinse and allow to air dry.
- .Store at room temperature 15-30°C (59-86°F)
- .Keep out of reach of children.
- .Use before the expiration date stamped on carton & bottle label.
- .LOBOB W/RW ~~Solution~~ ^{Drop} is not for use with soft (hydrophilic) contact lenses.

ADVERSE REACTIONS (PROBLEMS AND WHAT TO DO):

The following problems may occur while wearing contact lenses:

- .Redness of the eye
- .Eyes stinging, burning, or itching
- .Excessive watering (tearing) of the eyes
- .Unusual eye secretions
- .Reduced sharpness of vision (visual acuity)
- .Blurred vision
- .Sensitivity to light (photophobia)
- .Dry eyes

If you notice any of the above problems, IMMEDIATELY remove and examine your lenses. If the problem stops, and the lenses appear to be undamaged, thoroughly clean, rinse, and disinfect the lenses and reinsert them. If the problem continues, or a lens appears to be damaged, IMMEDIATELY remove your lenses and consult your eye care practitioner. DO NOT reinsert a damaged lens. If any of the above problems occur, a serious condition such as infection, corneal ulcer, neovascularization, or iritis may be present. Seek immediate professional identification and treatment of the problem to avoid serious eye damage. See your Instructions for Wearers Booklet for more information.

DIRECTIONS FOR USE:

General

- .Always wash and rinse your hands before handling your contact lenses.
- .Clean and rinse one lens, the right or left, first (always the same lens first to avoid mix-ups)

WETTING:

- .Remove the lens from the lens storage case and rinse thoroughly as directed by your eye care practitioner. It is important that this rinsing procedure is thorough. The lens should feel squeaky-clean between your fingers. If not, re-rinse the lens. All disinfecting and storage solution MUST be removed from the lens before wetting with LOBOB W/RW Solution and inserting the lens. ^{Drop}
- .Apply two drops of LOBOB W/RW ~~Solution~~ ^{Drop} over all surfaces of the lens WITHOUT rubbing the lens.
- .Insert the lens as instructed by your eye care practitioner.
- .Repeat the procedure with the other lens.
- .Empty your lens storage case, rinse under running hot tap

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water, and allow to air dry.

LUBRICATING:

When your lenses feel dry apply no more than two (2) drops of LOBOB W/RW ^{Drop} directly in the eye.

HOW SUPPLIED:

LOBOB W/RW ^{Drop} solution is supplied sterile in 1 fl. oz. (30 mL) ^{(and 0.3 fl. oz. (10 mL))} plastic bottles.

Bottles and cartons are marked with lot numbers and expiration date.

EACH CONTAINER IS TAMPER-EVIDENT SEALED. IF THE SEAL AROUND THE BOTTLE CAP IS MISSING OR BROKEN, DO NOT USE THIS PRODUCT

~~Manufactured - Distributed~~ by:

LOBOB LABORATORIES, INC. SAN JOSE, CALIFORNIA 95131

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