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Biomatrix, Inc.
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Ridgefield, New Jersey
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Tel 201 945 9550
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K994170

2.

510(k) SUMMARY

Hylashield® CL Lubricating Eye Drop
hylan fluid, 0.15%
Lubricant - Wetting/Rewetting Drop

1. SUBMITTER'S NAME
2. CONTACT PERSON AT BIOMATRIX, INC.
3. DATE THAT 510(k) SUMMARY WAS PREPARED
4. NAME OF THE MEDICAL DEVICE (Classification/Common/Proprietary)
5. LEGALLY MARKETED DEVICES TO WHICH SUBSTANTIAL EQUIVALENCE IS CLAIMED
6. DESCRIPTION OF THE DEVICE
7. INTENDED USE OF THE DEVICE
8. TECHNOLOGICAL COMPARISON BETWEEN SUBJECT AND PREDICATE DEVICES
9. SUMMARY OF PRECLINICAL SAFETY STUDIES AND CONCLUSIONS FROM PRECLINICAL SAFETY STUDIES
10. SUMMARY OF PRECLINICAL PERFORMANCE STUDIES
11. CLINICAL SAFETY AND EFFICACY STUDY

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| 1. SUBMITTER'S NAME |
| BIOMATRIX, INC. 65 Railroad Avenue Ridgefield, New Jersey 07657 USA |
| Tel: (201) 945-9550 Fax: (201) 945-0363 |

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| 2. U.S. REGULATORY CONTACT PERSON FOR BIOMATRIX, INC. |
| Nadine M. Qashu BIOMATRIX, INC. 65 Railroad Avenue Ridgefield, New Jersey 07657 USA |
| Tel: (201) 945-9550, ext. 202 Fax: (201) 945-0363 |

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| 3. DATE THAT 510(k) SUMMARY WAS PREPARED |
| November 22, 1999 |

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|--------------------------------------|---|
| 4. NAME OF THE MEDICAL DEVICE | |
| Classification name | Accessories to contact lenses – cleaning and wetting agents (86LPN) |
| Common / usual name | Lubricant - Wetting/Rewetting Drop |
| Proprietary name | Hylashield® CL Lubricating Eye Drop hylan fluid, 0.15% |

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| 5. LEGALLY MARKETED DEVICES TO WHICH SUBSTANTIAL EQUIVALENCE IS CLAIMED |
| <p>Wet-N-Soak® Rewetting Drops For use with rigid gas permeable contact lenses as a rewetting drop</p> <p>OPTIMUM by Lobob® Wetting/Rewetting Drops For use with fluoro-silicone acrylate, silicone acrylate and hard contact lenses as an in-the-eye lubricant and wetting/rewetting drop</p> |

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| 6. DESCRIPTION OF THE DEVICE |
| <p>Hylashield® CL Lubricating Eye Drop is a device that has not been previously cleared by FDA for different intended uses.</p> <p>Hylashield® CL Lubricating Eye Drop is a sterile, isotonic, preservative-free, clear, elastoviscous, ophthalmic solution presented in a single-use container. It contains hylan fluid, a viscous, elastic and biocompatible substance derived from the natural polysaccharide, hyaluronan. It lubricates and wets/rewets your lenses, thereby providing prolonged relief from symptoms of ocular discomfort associated with the use of rigid gas permeable contact lenses.</p> |

7. INTENDED USE OF THE DEVICE

Hylashield® CL Lubricating Eye Drop is intended to lubricate and wet/rewet rigid gas permeable contact lenses.

8. TECHNOLOGICAL COMPARISON BETWEEN SUBJECT AND PREDICATE DEVICES

Allergan markets *Wet-N-Soak® Rewetting Drops* and Lobob Laboratories markets *OPTIMUM by Lobob® Wetting and Rewetting Drop* for use with rigid gas permeable contact lenses. These predicate devices are indicated for relief of eye discomfort caused by wearing rigid gas permeable contact lenses. Hylashield® CL Lubricating Eye Drop is substantially equivalent to these products in that it has a similar intended use and indication.

The material from which Hylashield® CL Lubricating Eye Drop is made is different from the two predicate devices. Hylashield® CL Lubricating Eye Drop is composed of hylan fluid, whereas *Wet-N-Soak® Rewetting Drops* and *OPTIMUM by Lobob® Wetting and Rewetting Drops* are composed of hydroxyethylcellulose. *OPTIMUM by Lobob® Wetting and Rewetting Drop*, in addition, contains polyvinylpyrrolidone and polyvinyl alcohol. Hylan has been shown to be compatible with ocular structures and raises no new safety and efficacy issues. Also, a preservative is added to the two predicate devices, due to the fact that they are not supplied in a single-use container. Since Hylashield® CL Lubricating Eye Drop is supplied in a sterile, single-use container, it does not contain the preservatives that are used in the two predicate devices.

Hylashield® CL Lubricating Eye Drop is the same as *Wet-N-Soak® Rewetting Drops* and *OPTIMUM by Lobob® Wetting/Rewetting Drop* in that they are all supplied in the form of a sterile eye drop and serve as lubricants and wetting/rewetting drops for rigid gas permeable contact lenses. They are all made from materials which have demonstrated biocompatibility.

In conclusion, Hylashield® CL Lubricating Eye Drop has the same intended use as the marketed devices and differs only in the material from which it is made. All three devices are used to relieve eye discomfort caused by wearing rigid gas permeable contact lenses by wetting the lenses prior to insertion and by rewetting and lubricating the lenses while they are on the eye.

9. SUMMARY OF PRECLINICAL SAFETY STUDIES AND CONCLUSIONS FROM PRECLINICAL SAFETY STUDIES

Extensive *in vivo* animal and human use of hyaluronan and hylans have shown these products to be highly compatible for contact lens wearers. The studies contained in section A, ISO Biocompatibility Tests, were performed under and comply with the regulations outlined in 21 CFR Part 58 for Good Laboratory Practices.

A. ISO BIOCMPATIBILITY TESTS - Performed under GLP

Ref: International Standard ISO – 19033 (Biological Evaluation of Medical Devices)

1. SHORT TERM BIOLOGICAL TESTS

1.1 Irritation Tests

BXR 15202-F- Intracutaneous toxicity study in rabbit [hylan fluid]-GLP

Ocular Irritation:

BXR 50002-Eye Irritation Testing Protocol: Biomatrix Hylashield® 14-day Repeat Dose with Modified Hackett-McDonald Scoring-GLP

1.2 Sensitization and Immunogenicity Assays

BXR-10501-Dermal sensitization study (A Maximization Test) of hylan solution in the guinea pig -GLP

1.3 Cytotoxicity

BXR 15201-F- *In vitro* cytotoxicity study (MEM Elution Method) L-929 mouse fibroblast cell line [hylan fluid]-GLP

1.4 Acute Systemic Toxicity

BXR 15201-F Systemic toxicity study in mice [hylan fluid] (USP)-GLP

1.5 Hemocompatibility and Hemolysis

BXR 15200-F *In vitro* hemolysis study (direct contact method) [hylan fluid]-GLP

1.6 Pyrogenicity

BXR 15302-F – Rabbit pyrogen test of hylan fluid (USP)

1.7 Implantation

BXR 15204-F – USP muscle implantation study (with histopathology) in the rabbit (7 days) [hylan fluid]-GLP

BXR 15203-F – Muscle implantation study (with histopathology) in the rabbit (30 days) [hylan fluid] – GLP

1.8 Mutagenicity

BXR 10201-F – Ames mutagenicity test of hylan solution-GLP

2. LONG TERM BIOLOGICAL TESTS

2.1 Subchronic Toxicity

BXR 15303-2-F – Subchronic Two-Week Intraperitoneal Toxicity Study on Hylan A in Male Guinea Pigs [Effect of repeated intraperitoneal injections of hylan fluid (9.53 mg/ml) on blood parameters and histology of selected tissues in male guinea pigs] – GLP

BXR 15305-2-F – Subchronic Two-Week Intraperitoneal Toxicity Study on Hylan A Female Guinea Pigs [Effect of repeated intraperitoneal injections of hylan fluid (10mg/ml) on blood parameters and histology of selected tissue - GLP

**9. SUMMARY OF PRECLINICAL SAFETY STUDIES AND CONCLUSIONS
FROM PRECLINICAL SAFETY STUDIES (continued)**

BXR 15209-F – Subchronic One-Month Intra-Arterial Toxicity Study on Hylan A in Male Rabbits [Effect of intra arterial injections of hylan fluid (1 mg/ml, 3 mg/kg) on hematology and blood chemistry, blood hyaluronan content, and histology of selected tissue in male rabbits] – GLP

BXR 15303-F – Subchronic One-Month Intra-Articular Toxicity Study on Hylan A in Male Rabbits [Effect of repeated intra-articular application of hylan fluid (3.54 mg/ml) on joint biochemistry, hematology, and blood chemistry in rabbits] – GLP

2.2 Reproduction Studies

BXR 12243-F – Effect of Intra-ocular Implantation of Hylan Fluid, Hylan Gel, Hyaluronan and Hylan G-F 20 on the Reproductive Capacity of Owl Monkeys: A Retrospective Study.

3. PHARMACOKINETICS

BXR 15211-F – Clearance of hylan fluid after intra-articular injection into rabbit knees as Determined by radiotracer studies

BXR 15215-F – Clearance of hylan fluid after direct intravascular administration

A. BASIC EXPLORATORY STUDIES (SUPPORTIVE STUDIES)

1. SHORT TERM BIOLOGICAL STUDIES

1.1 Acute Systemic Toxicology

BXR 15208-F – Effect of single intra-articular injection (0.3 ml) of hylan fluid (5 mg/ml) on joint biochemistry

BXR 15208-2-F – Effect of single large volume (0.5 ml) intra-articular application of hylan fluid (10 mg/ - joint histology/biochemistry)

BXR 15408-F – Effect of single intra-articular application of hylan fluid (10 mg/ml) on joint histology in female rabbits

BXR 15311-F – Histology studies of rabbit joint tissues one and four weeks after single Intra-articular administration of 0.3 ml hylan fluid (5 mg/ml)

BXR 15308-F – Effect of single large volume (2.0 ml) intra-articular application of hylan fluid on joint biochemistry

1.2 Hemocompatibility and Hemolysis

BXR 12203-F – Rabbit blood hemolysis test of hylan fluid

BXR 12205-F – Rabbit blood hemolysis: hylan fluid extracts

BXR 12216-F – Partial thromboplastin time: effect of hylan fluid

BXR 12217-F – Platelet activation studies: *in vitro* effect of hylan fluid

**9. SUMMARY OF PRECLINICAL SAFETY STUDIES AND CONCLUSIONS
FROM PRECLINICAL SAFETY STUDIES (continued)**

1.3 Implantation

BXR 15310-B-F – Implantation of hylan fluid into the intra-vitreous space of primate eyes:
short term evaluation

BXR 15310-A-F – Implantation of hylan fluid into the intra-vitreous space of primate eyes:
long term evaluation

2. LONG TERM BIOLOGICAL TESTS

Subchronic Toxicity

BXR 10522-F – Short term toxicity testing of hylan fluid in rats; administration by weekly
Intra-peritoneal injection

BXR 15406-F – Effect of repeated intra-articular application of hylan fluid on joint histology
of female rabbits

3. Reproduction Studies

BXR 15320-F – Effect of hylan fluid on fertility and pregnancy in horse

10. IN VIVO TEST OF EFFICACY

BXR 15501 – Effect of Hylan Fluid on Fluorescein Break-Up-Time (FBUT) and Drying Time in
Owl Monkey Eyes

Summaries and conclusions of all the above studies are included in the Biocompatibility
Section of this document.

11. CLINICAL SAFETY AND EFFICACY STUDY

The safety and efficacy of Hylashield[®] CL Lubricating Eye Drop as a lubricating and wetting/rewetting agent was compared to one of the predicate devices, Wet-N-Soak[®], in minimizing daily discomfort associated with rigid gas permeable (RGP) contact lenses in this study. These products were evaluated in conjunction with the two most commonly used RGP lens types. The analysis of the clinical study data showed the substantial equivalence of Hylashield[®] CL Lubricating Eye Drop with Wet-N-Soak[®] with regard to slit lamp findings, symptom/problems/complaints, visual acuity, average wear time and lens replacement. The high patient compliance rate and extremely low rate of adverse events in both treatment groups indicated that Hylashield[®] CL Lubricating Eye Drop is well tolerated and safe when compared to Wet-N-Soak[®].

In conclusion, the data from this report demonstrated that Hylashield[®] CL Lubricating Eye Drop is substantially equivalent to its predicate device, Wet-N-Soak[®] with respect to safety and effectiveness as a lubricating and wetting/rewetting agent to provide prolonged relief from symptoms of ocular discomfort associated with the use of RGP contact lenses. Wet-N-Soak[®] has the same intended use as OPTIMUM by Lobob[®] Wetting and Rewetting Drop.



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Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Ms. Nadine M. Qashu
Director, Regulatory Affairs
Biomatrix, Inc.
65 Railroad Avenue
Ridgefield, New Jersey 07657

Re: K994170
Trade Name: Hylashield CL Lubricating Eye Drops
Regulatory Class: II
Product Code: 86 MRC
Dated: December 10, 1999
Received: December 10, 1999

Dear Ms. Qashu:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Pre-market Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic (QS) inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4613. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>".

Sincerely yours,



A. Ralph Rosenthal, M.D.

Director

Division of Ophthalmic Devices

Office of Device Evaluation

Center for Devices and

Radiological Health

Enclosure

1. Statement of Indications for Use:

Application: Biomatrix, Inc.

510(K) Number (if known): K994170

Device Name: Hylashield® CL Lubricating Eye Drops

Indications for Use: Hylashield® CL Lubricating Eye Drops are indicated for lubricating and wetting/rewetting rigid gas permeable contact lenses.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use _____ or Over-the-Counter Use X

(per 21 CFR 886.5918)

(Optional Format 1-2-96)

James W. C. Brown, M.D.

JS

(Division Sign-Off)
Division of Ophthalmic Devices

510(k) Number K994170