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K993362

2.

510(k) SUMMARY

Hylasine™, hylan B gel
(77 EMX)

510(k) Summary Sections:

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
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10. SUMMARY OF PRECLINICAL PERFORMANCE STUDIES
11. CLINICAL SAFETY AND EFFICACY STUDY

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

2. U.S. REGULATORY CONTACT PERSON FOR BIOMATRIX, INC.
Mario J. Reres Vice President, Regulatory Affairs BIOMATRIX, INC. 65 Railroad Avenue Ridgefield, New Jersey 07657 USA
Tel: (201) 945-9550, ext. 270 Fax: (201) 945-0363

3. *DATE THAT 510(k) SUMMARY WAS PREPARED*
October 1, 1999

4. *NAME OF THE MEDICAL DEVICE*	
Classification name	Balloon, epistaxis (nasal) (Ear, Nose & Throat 77 EMX)
Common / usual name	Epistaxis Balloon
Proprietary name	Hylasine™

5. *LEGALLY MARKETED DEVICES TO WHICH SUBSTANTIAL EQUIVALENCE IS CLAIMED*
Xomed MeroGel™ Nasal Dressing and Sinus Stent (Xomed, K982732) ENTaxis™ Nasal Packing (Laboratoires Brothier S.A., K984069) Merocel® Nasal Dressing (Merocel Corp., K920394)

6. *DESCRIPTION OF THE DEVICE*
Hylasine™ is a sterile, transparent, viscoelastic gel composed of cross-linked polymers of hyaluronan. Due to its physical properties, Hylasine may be used to reduce synechiae and middle meatal stenosis. Its tamponade effect may also contribute to controlling bleeding. Hylasine leaves the site of placement by natural elimination, or it may be aspirated from the cavity earlier at the discretion of the physician.

7. *INTENDED USE OF THE DEVICE*
The intended use of Hylasine™ is for use in nasal/sinus cavity as a space-occupying gel stent, to separate mucosal surface and to help control minimal bleeding following surgery or nasal trauma.

8. *TECHNOLOGICAL COMPARISON BETWEEN SUBJECT AND PREDICATE DEVICES*

Xomed markets *MeroGel™ Nasal Dressing and Sinus Stent* and *Merocel® Doyle Nasal Dressing* and Laboratoires Brothier S.A. markets *ENTaxis™ Nasal Packing* for use in nasal sinus cavity as space-occupying stent, to separate mucosal surface and/or to help control minimal bleeding following surgery or nasal trauma. These predicate devices are indicated for use in nasal/sinus surgery and/or trauma. Hylasine™ is substantially equivalent to these predicate products in that it has a similar intended use and indications across the three products. The subject and predicate devices are made from materials which have demonstrated satisfactory biocompatibility, are highly absorbent for collecting postop fluids and are sterile single use.

Hylasine™ is different from ENTaxis™ in the material from which it is made – Hylasine™ being composed of hylan B gel and ENTaxis™ being composed of calcium alginate fibers. Hylan B has been shown as biocompatible and raises no new issue of safety or effectiveness.

Hylasine™ is different from Merocel® also in the material from which it is made – Merocel® being composed of hydroxylated polyvinyl acetal. Both products have a tamponade effect, Hylasine™ in the sinus cavities and Merocel® in the nasal passages, following surgery.

Hylasine™ and MeroGel™ are both made from derivatives of hyaluronic acid; the form of the product is different. Hylasine™ is introduced into the sinus cavities as a gel whereas MeroGel™ changes from its original form of a white fibrous material with a physical appearance similar to spun cotton, to a gelatinous mass once it is introduced into the nasal/sinus cavities. Due to its pseudoplastic properties, hylan B (which makes up Hylasine™) can be easily inserted and removed from the passageways, although hylan B also leaves the site of placement via normal outflow channels. Animal and clinical studies showed no toxic reaction to hylan B.

In conclusion, Hylasine™ has the same intended use as the marketed devices and differs only in the material or form of the material. All four devices are used during surgery and/or post-surgically to prevent adhesions and/or to control bleeding.

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

Hylasine™ has been evaluated through *in vitro* tests and animal safety studies. All of these results are consistent in indicating that this product is safe for use as a sinus gel. Summaries of the studies listed below are included in the Biocompatibility Section (Section 7) of this 510(k) Notification.

A. TRIPARTITE NONCLINICAL STUDIES (GLP)

1. SHORT TERM BIOLOGICAL TESTS

1.1 Irritation Tests

BXR 25204-F-I GLP - Intracutaneous Toxicity Study in the Rabbit
NAmSA # 93T-05713-00

BXR 23004-I GLP - Subcutaneous Implantation Study (With Histopathology) In the Rabbit (2 Days)
NAmSA # 94T-01840-00, 94T-01840-01

1.2 Sensitization and Immunogenicity

BXR 23006-I GLP - Immunization and Subchronic Intramuscular Toxicity Study of Hylan B, Collagen I (Zyplast®) or Collagen II (Zyderm II®) in Rabbits. (TSI # 005-0001)

BXR 20501-F-I GLP - Dermal Sensitization Study (A Maximization Test) in the Guinea Pig of Hylan Gel Degraded
NAmSA # 87T-157370-00

BXR 20008-I GLP - Delayed Contact Sensitization Study (A Maximization Method) in the Guinea Pig (Hylan B Gel)
NAmSA # 95T-09406-00

1.3 Cytotoxicity

BXR 25203-F-I GLP - *In Vitro* Cytotoxicity (MEM Elution Method) Study in the L929 Mouse Fibroblast Cell Line
NAmSA # 93T-05712-00

BXR 23005-I GLP - *In Vitro* Cytotoxicity Study (Agarose Overlay Method) in the L929 Mouse Fibroblast Cell Line
NAmSA # 94T-01840-00

1.4 Acute Systemic Toxicity

BXR 25200-F-I GLP - Systemic Toxicity Study in Mice
NAmSA # 93T-05713-00

1.5 Hemocompatibility and Hemolysis

BXR 25202-F-I GLP - *In Vitro* Hemolysis Study (Direct Contact Method)
NAmSA # 93T-05712-00

1.6 Pyrogenicity

BXR 20001-I GLP - USP Rabbit Pyrogen Study
(NAmSA 94T-12580-00)

BXR 20002-I GLP - USP Rabbit Pyrogen Study
(NAmSA 94T-12581-00)

BXR 20003-I GLP - USP Rabbit Pyrogen Study (NAmSA 94T-12582-00)

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

1.7 Implantation

BXR 23003-I GLP - Muscle Implantation Study (With Histopathology) in the Rabbit (7 Days)
NAmSA # 94T-01840-00, 94T-01840-01

BXR 25201-F-I GLP - USP Muscle Implantation Study (With Histopathology) in the Rabbit (7 Days)
NAmSA # 93T-05714-00

BXR 25205-F-I GLP - Muscle Implantation Study (With Histopathology) in the Rabbit (30 Days). NAmSA # 93T-05715-00

1.8 Mutagenicity

BXR 20202-F-I GLP - Ames Mutagenicity Test of Hylan Gel (Degraded)
NAmSA Lab 87T-15737-00

BXR 20201-F-I GLP - Ames Mutagenicity Test of Hylan Gel
NAmSA Lab 87T-15738-00

BXR 23000-I GLP - Test For Chemical Induction of Gene Mutation at the HGPRT Locus in Cultured Chinese Hamster Ovary (CHO) Cells With and Without Metabolic Activation
SITEK # 0265-2510

BXR 23001-I GLP - Test For Chemical Induction of Chromosome Aberration in Cultured Chinese Hamster Ovary (CHO) Cells With and Without Metabolic Activation
SITEK # 0265-3113

BXR 23002-I GLP - Test For Chemical Induction of Morphological Cell Transformation in Cultured BALB/C-3T3 Cells With and Without Metabolic Activation
SITEK # 0265-6100

2. LONG TERM BIOLOGICAL TESTS

2.1 Subchronic Toxicity

BXR 25305-F-I GLP - Subchronic Two-Week Intraperitoneal Toxicity Study on Hylan Gel in Male Guinea Pigs [Short Term Chronic Toxicity Testing of Hylan Gel in Male Guinea Pigs]

BXR 23006-I GLP - Immunization and Subchronic Intramuscular Toxicity Study of Hylan B, Collagen I (Zyplast®) or Collagen II (Zyderm II®) in Rabbits.
(TSI # 005-0001)

2.2 Chronic Toxicity and Carcinogenicity

BXR 25405-F-I GLP - One Year Subcutaneous Toxicity Study on Hylan B in Female Rats

2.3 Reproduction Studies

BXR 12243-F-I - Effect of Intraocular Implantation of Hylan Fluid, Hylan Gel, Hyaluronan and Hylan G-F 20 on the Reproductive Capacity of Owl Monkeys: A Retrospective Study (General Reproduction Study (Segment I) of the Effect of Intraocular/Intra-articular Injection of Hyaluronan, Hylan A, Hylan B and Synvisc® (hylan G-F 20) in Owl Monkeys)

3. PHARMACOKINETICS

BXR 25407-F-I - Intradermal Injection Of [^{3}H]-Hylan B ([^{3}H]-hylan gel) in Guinea Pigs

BXR 25213-I Six Month Study of Residence Time of [^{14}C]-Hylan B After Intradermal Administration in Female Guinea Pigs

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

3. PHARMACOKINETICS (continued)

BXR 25212-F-I - Distribution of [^{3}H]-Hylan Gel (Degraded) in Rats
(TSI MRI # 2-339)

B. BASIC EXPLORATORY STUDIES (SUPPORTIVE STUDIES)

1. SHORT TERM BIOLOGICAL TESTS

1.1 Acute Irritation

BXR 25302-F-I - Effect of Intradermal Administration of Hylan Gel on Local Tissue Reaction in Nu-Nu Nude Mice

BXR 25407A-F-I - Histology of Rabbit Conjunctiva After Subconjunctival Implantation of Hylan Gel

1.2 Sensitization/Immunization Studies

BXR 20004-I - The Immunogenicity AXHA [Hylan Gel] in Rabbits
Bard Protocol A9203

BXR 20006-I - Immunogenicity Study of Two Biomaterials [Hylan Gel and Collagen] in Rabbits
Bard Protocol A902

BXR 20005-I - Immunogenicity Study of Two Biomaterials [Hylan Gel and Collagen] in Rabbits
Bard Protocol A915

BXR 22222-F-I - Immunogenicity of Hylan Gel in Rabbits as Demonstrated by Passive Cutaneous Anaphylaxis in Guinea Pigs

BXR 22220-F-I - Intravitreal Hylan Gel in Owl Monkeys: Skin Testing Via Intradermal Injection of Hylan Gel and Measurement of Serum Antibodies

BXR 22227-F-I - Human Complement Activation: Effect of 4 Batches of Hylan Gel, Both Nondegraded and Sonically Degraded

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

1.3 Cytotoxicity

BXR 26101-F-I - The Effect of Hylan Gel on Corneal Endothelial Function

BXR 22202-1-F-I - Agar Overlay Tissue Culture Toxicity Testing of Degraded and Undegraded Hylan Gel

BXR 22202-2-F-I - Agar Overlay Tissue Culture Toxicity Testing of Hylan Gel Extracts

BXR 22214-F-I - Endothelial Cell Cytotoxicity of Hylan Gel Which Was Undegraded or Degraded By Hyaluronidase or Sonication

BXR 22223-F-I - Inhibition of Cell Growth Test: Evaluation of Hylan Gel

BXR 22224-F-I - Inhibition of Cell Growth Test: Evaluation of Hylan Gel

1.4 Acute Systemic Toxicity

BXR 25209 -F-I - Effect of Intra-Arterial Injection of Degraded Hylan Gel (3 mg/ml) on Hematology and Blood Chemistry, Blood Hyaluronan Content and Histology of Selected Tissues of Male Rabbits

1.5 Hemocompatibility and Hemolysis

BXR 22203-F-I - Rabbit Blood Hemolysis Test of Hylan Gel

BXR 22205-F-I - Rabbit Blood Hemolysis Test: Hylan Gel Extracts

BXR 22216-F-I - Partial Thromboplastin Time (PTT): Effect of Hylan Gel

BXR 22217-F-I - Platelet Activation Studies: Effect of Hylan Gel

1.6 Pyrogenicity (rabbit)

BXR 25313-F-I - Rabbit Pyrogen Test of Hylan Gel (USP)

1.7 Implantation

BXR 25087-F-I - The Use of Hylan Gel in Filtering Surgery: Trabeculectomy Studies in Owl Monkeys

BXR 25311-I - Long-Term Compatibility of Hylan Gel With Retinal Function in Owl Monkey Eyes: Dark-Adapted ERG Study

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

2. LONG TERM BIOLOGICAL TESTS

BXR 25408-F-I - Intradermal and Subcutaneous Injection of Hylan Gel in Guinea Pigs

BXR 25310-C-F-I - Hylan Gel Implantation into the Intravitreal Space of Primate Eyes: Long Term Observation

BXR 25411-I Comparative Study of Two Biomaterials [Hylan Gel Autoclaved and Nonautoclaved] and Related Tissue Responses in Rabbits - [Bard Protocol A903]

BXR 25410-I - Comparative Studies of Intradermal, Intramuscular, and Periurethral - Bladder Neck Tissue Responses to Three Biomaterials

3. PHARMACOKINETICS

BXR 105-G-I - Clearance of Hylan Gel from the Joint and the Blood

10. *SUMMARY OF PRECLINICAL PERFORMANCE STUDIES*

BXR 20007-I - The Use of Hylasine™, Hylan B Gel, in Sinonasal Surgery: A Pilot Study (Rabbits)

BXR 20010-I - The Influence of Hylan Gel (Hylan B) on the Healing of Full Thickness Excision Dermal Wounds in Guinea Pigs

Summaries of the studies listed above are included in the Biocompatibility Section (Section 7) of this 510(k) Notification.

11. *CLINICAL SAFETY AND EFFICACY STUDY*

Hylasine™ has been clinically evaluated as a surgical adjunct in endoscopic sinus surgery. Results indicate that this product is safe and effective for this use.

Hylasine™ treatment was compared with no treatment in the contralateral sinus in a total of 30 patients undergoing bilateral ethmoidectomy at three centers. The data clearly show support for the superiority of Hylasine™ over no treatment in the control of synechiae/adhesions and middle meatal stenosis. Hylasine™ also showed a favorable effect over no treatment in mucosal status and regeneration as compared to the contralateral side at certain time points. This suggests a better, unimpeded healing process for Hylasine™-treated tissue. Hylasine™ was also judged as somewhat or very effective in the stilling of operative bleeding in 19 of the 20 patients where this was measured.

The clinical studies demonstrated that Hylasine™ can significantly help to reduce the formation of synechiae/adhesions, improve middle meatal stenosis, allow for unimpeded tissue healing and still operative bleeding which can occur during and/or after endoscopic sinus surgery. The safety profile of Hylasine™ showed that the product was well-tolerated.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

MAR 13 2000

Mr. Mario J. Reres
Vice President, Regulatory Affairs
Biomatrix
65 Railroad Avenue
Ridgefield, New Jersey 07657 USA

Re: K993362
Trade Name: Hylasine™
Regulatory Class: I
CFR: 874.4100
Product Code: 77EMX
Dated: February 9, 2000
Received: February 10, 2000

Dear Mr. Reres:

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 (Premarket 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:

Applicant: Biomatrix, Inc.

510(k) Number (if known): K993362

Device Name: Hylasine™

Indications for Use: The intended use of Hylasine™ is for use in nasal/sinus cavity as space-occupying gel stent, to separate mucosal surface and to help control minimal bleeding following surgery or nasal trauma.

(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 _____

(Per 21 CFR 801.109) (Optional Format 1-2-96)

(Division Sign-Off)
Division of Ophthalmic Devices
510(k) Number K993362