

JUL - 6 1999

K982180

Integra LifeSciences Corporation
510(k) K982180
DuraGen™ Dural Graft Matrix

**510(k) PREMARKET NOTIFICATION
SUMMARY OF SAFETY AND EFFECTIVENESS**

**In Accordance with the
Safe Medical Device Act of 1990**

DuraGen™ Dural Graft Matrix

1. Submitted by:

Integra LifeSciences Corporation
105 Morgan Lane
Plainsboro, NJ 08536
USA
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Contact Person:

Judith E. O'Grady, RN, MSN, RAC
Sr. Vice President, Regulatory Affairs
(609) 936-2311

2. Date Prepared: June 1, 1999

3. Name of the Medical Device:

Proprietary Name: DuraGen™ Dural Graft Matrix
Classification Name: Dura Substitute

4. Device Classification:

Class II
Regulation Number 21 CFR 882.5910

5. Indications for Use

- DuraGen™ Dural Graft Matrix is indicated as a dura substitute for the repair of dura mater.

6. Statement of Substantial Equivalence

DuraGen™ Dural Graft Matrix is substantially equivalent in function and intended use to the following devices:

- I.yoplast® Dura Substitute, (Bovine Pericardium), 510(k) K970851
Manufactured for AESCULAP, Inc.
- Dura-Guard® Dural Repair Patch, (Bovine Pericardium), 510(k) K973706
Manufactured by BioVascular, Inc.
- Preclude® Dura Substitute, (Expanded polytetrafluoroethylene),
510(k) K953967.
Manufactured by W.L. Gore & Associates

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- d. TutoPlast® Processed Dura Mater, (Human Dura Mater), 510(k) K910555
Manufactured by Biodynamics International, Inc.
- e. Lyodura®, (Human Dura Mater)
Manufactured for AESCULAP, Inc.

7. **Device Description**

DuraGen™ *Dural Graft Matrix* is an absorbable implant for repair of dura mater. DuraGen™ is an easy to handle, soft, white, pliable, nonfriable, porous collagen matrix. DuraGen™ is supplied sterile, nonpyrogenic, for single use in double peel packages in a variety of sizes.

DuraGen™ is manufactured from bovine achilles tendon, which is classified by European Standards as Class IV material, no detectable infectivity for Bovine Spongiform Encephalopathy (BSE). The bovine tendon is known to be one of the purest sources of Type I Collagen that is commercially available. The collagen used to manufacture DuraGen™ is currently used in the manufacture of an artificial skin, absorbable hemostatic sponges, and absorbable wound dressings. The manufacturing process for DuraGen™ meets the United States Food and Drug Administration's Guidance document and European Standards for animal tissue sourcing, handling and inactivation of BSE. This process involves a treatment with sodium hydroxide that is a recognized method of inactivation of Spongiform Encephalopathy (SE). The bovine tendon is only obtained from facilities in the United States of America that have been inspected by the United States Department of Agriculture (USDA). Bovine Spongiform Encephalopathy (BSE) is not known to exist in the United States of America, therefore, the United States of America is considered by the European Union as a low risk country for bovine sourced materials.

A viral inactivation study for the DuraGen™ manufacturing process was conducted by an independent certified laboratory. In this study, the sodium hydroxide treatment was evaluated for its ability to inactivate the following viral strains: Human Immunodeficiency Virus Type I (HIV), Bovine Viral Diarrhea (BVD), Infectious Bovine Rhinotracheitis (IBR), Parainfluenza Virus Type 3 (P13), Vesicular Stomatitis (VSV). For these viruses, the sodium hydroxide treatment reduced the viral titer to non-detectable levels.

8. **Performance Data**

DuraGen™ *Dural Graft Matrix* has been evaluated by a number of tests for safety, biocompatibility, toxicity, pyrogenicity, sterility and preclinical and clinical evaluations. Summaries and reports of all data are contained in the Premarket Notification submission.

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Biocompatibility

The biocompatibility studies have demonstrated DuraGen™ *Dural Graft Matrix* to be: noncytotoxic, nonpyrogenic, nonmutagenic, nonsensitizing and be absorbed with no cellular or allergic responses. The following studies were conducted:

- Cytotoxicity
- Irritation/Intracutaneous Reactivity
- Pyrogenicity
- Genotoxicity
- Sensitization Study
- Chronic Toxicity Study
- Implantation Studies
- Intramuscular Toxicity Study
- Subcutaneous Implantation Study
- Immunological/Sensitivity Studies
- Mechanical Testing

Clinical Studies

The collagen sponge was evaluated in a long-term clinical study to examine its suitability as a dural graft. Clinical evaluations involving more than 1,000 patients demonstrated that DuraGen™ Dural Graft Matrix performed safely and effectively as a dura substitute. During the course of the study, biopsies of the collagen implant were available from 100 patients for macroscopic and histological examination. There were no incidences of graft encapsulation, neomembrane formation, delayed hemorrhage, or foreign body reactions.

9. Summary/Comparison of Technological Characteristics

Technological Characteristics

DuraGen™ and its predicates have similar technological characteristics.

The technological differences between DuraGen™ and the predicate devices do not raise new types of safety or effectiveness issues. The technological differences have been assessed by valid scientific and clinical methods. Physical, laboratory, animal and human clinical test methods have been performed and have proven the ability of DuraGen™ to function as a dura substitute.

Table 1 describes the properties of DuraGen™ *Dural Graft Matrix* compared to properties of the predicate devices.

10. Manufacturing

DuraGen™ *Dural Graft Matrix* is manufactured by Integra LifeSciences Corporation at its facility in Plainsboro, NJ in compliance with FDA Quality System Regulations. The facility is registered as a United States Food and Drug Administration Medical Device manufacturing facility. The Integra LifeSciences facility is also ISO 9001/EN 46001/Medical Device Directive certified.

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The collagen used to manufacture DuraGen™ is used in other implantable medical devices manufactured by Integra LifeSciences such as hemostatic sponges, implantable wound dressings, and artificial skin.

11. Quality Assurance

DuraGen™ is fully tested according to an established Quality Control procedure and is only released if the product conforms to specifications.

The test data from extensive *in vito and in vivo* preclinical testing and extensive human clinical studies presented in this submission establish that DuraGen™ *Dural Graft Matrix* is equivalent to predicate devices in biocompatibility and safety and effectiveness as a dura substitute.

TABLE 1: Substantial Equivalence Comparison Chart

| Feature | DuraGen™ Dural Graft Matrix | Lyoplant® Dura Substitute¹ | Lyodura®¹ | Dura-Guard®- Dural Repair Patch¹ | Preclude® Dura Substitute¹ | Tutoplast® Dura Substitute¹ |
|--------------------------------------|--|---|---|--|--|---|
| Manufacturer/ Distributor | Integra LifeSciences Corporation | B. Braun /Aesculap | B. Braun/Aesculap | Bio-Vascular, Inc. | W.L. Gore & Associates, Inc. | Biodynamics, Inc. |
| Indications for Use | Dura Substitute Used as a dura substitute for the repair of dura mater. | Dura Substitute Used as a dura mater substitute in neurological procedures for soft tissue reconstruction of damaged, impaired, or missing tissue. | Dura Substitute Indicated for the replacement and enlargement of connective-tissue structures. | Dura Substitute Used as a dural substitute for the closure of dura mater during neurosurgery. | Dura Substitute Used as a dura substitute and for spinal membrane | Dura Substitute Used as a substitute for human dura mater. |
| Materials | Bovine Type I Collagen | Bovine pericardium | Human Dura Mater | Bovine pericardium | Expanded polytetrafluoroethylene | Human Dura Mater |
| Absorption Time | Gradual biodegradation | Gradual biodegradation | Information not available | Gradual biodegradation | Non-resorbable | Gradual biodegradation |
| Non-Pyrogenic | YES | YES | YES | Not claimed | YES | YES |

¹Based on information from company brochure



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Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Ms. Judith E. O'Grady, RN, MSN
Senior Vice President
Regulatory Affairs, Quality Assurance and Clinical Affairs
Integra Life Sciences Corporation
105 Morgan Lane
Plainsboro, New Jersey 08536

Re: K982180
Trade Name: DuraGen™ Dural Graft Matrix
Regulatory Class: II
Product Code: GXQ
Dated: June 1, 1999
Received: June 3, 1999

Dear Ms. O'Grady:

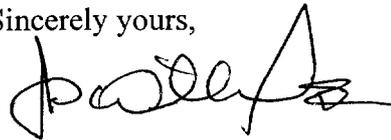
We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of 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 requirement, 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) 594-4595. 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,



f Celia M. Witten, Ph.D., M.D.
Director
Division of General and
Restorative Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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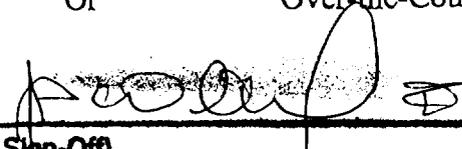
Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use
(Per 21 CFR 801.109)

Or

Over-the-Counter Use

Optional Format 1-2-96)



(Division Sign-Off)
Division of General Restorative Devices
510(k) Number _____

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