

NOV 25 1998

K983009

510(k) SUMMARY α -BSM™ Bone Substitute Material for Cranioplasty

1. SUBMITTER INFORMATION

- 1.1 Name: ETEX Corporation
- 1.2 Address: ETEX Corporation
University Park at MIT
350 Massachusetts Avenue, 4th Floor
Cambridge, Massachusetts 02139 U.S.A.
- 1.3 Telephone: 617-577-7270
FAX: 617-577-7170
- 1.4 Contact: Michael Schuttenberg
Director, Quality Assurance / Regulatory Affairs
- 1.5 Summary
Preparation Date: Monday, November 16, 1998

2. DEVICE INFORMATION

- 2.1 Proprietary Name: α -BSM™ Bone Substitute Material for Cranioplasty
- 2.2 Common Names: Bone Graft Material, Bone Cement, Bone Substitute Material
- 2.3 Classification
Name and Code: Methyl Methacrylate for Cranioplasty, Code GXP
- 2.4 Predicate Device: BoneSource™ Hydroxyapatite Cement
510(k) No.: K953339, Osteogenics, Inc.
- 2.5 Description of Device

ETEX α -BSM™ Bone Substitute Material for Cranioplasty is a self-setting, synthetic calcium phosphate hydroxyapatitic powder that hardens in an aqueous environment at body temperature. The α -BSM™ powder is mixed with saline at the time of use and the resulting paste is applied directly to the defect site. Prior to implantation, it remains moldable for several hours. After implantation, the material hardens in approximately one hour. The material is dimensionally stable during setting, and has been demonstrated to be highly biocompatible with mammalian tissues. After implantation, the material resorbs and is replaced by natural bone.

As supplied, each transparent plastic pouch of α -BSM™ Bone Substitute Material contains a unit dose of sterile α -BSM™ Bone Substitute Material (dry white powder) contained within an elastomeric mixing bulb (available in 0.5, 1.0, 2.5, 5.0, 10 and 25 gram dose sizes); a sterile syringe, a 16 gauge needle, and a vial containing sterile saline; and Instructions for Use. The saline is injected aseptically into the mixing bulb and the material is mixed by kneading the bulb with the fingers. The material can be shaped into the desired form prior to application or shaped *in situ* in the defect. α -BSM™ Bone Substitute Material is synthesized from reagent grade inorganic raw materials composed of salts of calcium and phosphates. There are no substances of biological origin used in the synthesis or processing of the product. No additional preservatives or medicinal substances are present.

2.6 Intended Use

α -BSM™ Bone Substitute Material is a synthetic calcium phosphate hydroxyapatitic material intended to be implanted for use in the filling, repair, reconstruction and augmentation of burr holes, contiguous craniotomy cuts, and other defects in craniofacial bones including fronto-orbital, malar and mental areas with a surface area no larger than 25cm².

It is intended for single use, permanent implantation. It is supplied in sterile kit form, and is not intended to be resterilized. Use of α -BSM™ Bone Substitute Material with other legally marketed devices for these indications has not yet been evaluated. α -BSM™ Bone Substitute Material is not designed or sold for any use except as indicated.

2.7 Substantial Equivalence to Predicate Device

α -BSM™ Bone Substitute Material is believed to be substantially equivalent to BoneSource™ in terms of design, materials, function, and intended use. Both materials are sterile, self-setting calcium phosphate powders that cure into hydroxyapatite after addition of an aqueous vehicle. This similarity in composition results in a similar degree of biocompatibility for both products. Both materials set in nonexothermic reactions. Both materials are intended for non-load-bearing bone defect filling indications in the craniofacial area. The information below briefly discusses those tests performed that support a determination of substantial equivalence.

3. TESTING USED FOR SUBSTANTIAL EQUIVALENCE EVALUATION

3.1 Physico-Chemical Testing

Analyses were performed on the predicate device to determine its chemical and crystalline composition relative to the characterization of α -BSM™ Bone Substitute Material. These tests included Fourier Transformed Infrared Spectroscopy, X-ray Diffraction Analysis, Calcium: Phosphorus ratio, Solubility Determination and mechanical properties. Comparison of the results of these tests indicate very similar composition, nearly identical crystallinity, and similar solubility - both materials are very nearly insoluble.

Both materials consist of salts of calcium phosphate which, when mixed in an aqueous environment and allowed to harden at body temperature, cure into hydroxyapatite in nonexothermic reactions. Comparing infrared spectroscopy results of both products supports the premise that the type and level of chemical bonding is very similar between the two products. In X-ray Diffraction analysis of the two products, comparison demonstrates that both materials are composed of Hydroxyapatite in the crystalline phase and largely predominant portion of the samples, with both containing an amorphous component. Calcium : phosphorus ratios of the two products were determined and found to be similar. A comparison of solubility properties of the two products was made on hardened samples under simulated physiologic conditions. The results indicate that both materials are only slightly soluble. ETEX believes these results are strongly suggestive of chemically and physically equivalent products.

3.2 Biocompatibility

A variety of tests and evaluations were performed on α -BSM™ to ascertain possible effects of the introduction of this material into mammalian systems or tissues. The tests performed and brief results or conclusions are listed below.

Mutation Assay (Ames Test)

No increase in mutation reversion frequencies were observed.

Micronucleus Test

No clastogenic effects (chromosome breakage) were noted.

Hemolysis Assay

No negative effects observed. In fact, α -BSM™ treated samples showed a decrease in hemolysis.

MEM Elution Test

This test of cytotoxicity showed no negative effects.

USP Systemic Toxicity Test

No negative systemic effects observed.

Delayed Contact Sensitization Test

This test of skin sensitization showed no effects beyond that of control articles.

Pyrogen Test

α -BSM™ was determined to be nonpyrogenic by the rabbit pyrogen test.

Intracutaneous Toxicity Test

After injection of α -BSM™ extracts, there was no evidence of irritation or toxicity beyond that of control articles.

Muscle Implantation

Two weeks after implantation of α -BSM™ into rabbit muscle sites, there was no macroscopic evidence of tissue irritation. Microscopic evaluation showed slight cellular effects when compared with control articles.

Bacterial Endotoxin (LAL) Evaluation

This alternate method of testing for pyrogenic effects of an article showed no measurable endotoxins in α -BSM™, and demonstrated that the product did not artificially affect the test results by inhibition or activation of the reagents used.

Chronic Safety/Efficacy Study

One year after implantation of α -BSM™ into surgically created bone defects in dog femurs, clinical and histopathologic evaluation of the repair sites demonstrated that new bone growth had occurred to an extent equal to that of autografts, and included remodeling of the bone tissue. There were no significant adverse findings.

Histology and Histomorphometry Evaluation

A comparative *in vivo* study with α -BSM™ and autograft implanted into a canine femoral defect model demonstrated equivalent new bone replacement of the implant material at each timepoint for this one year study.

Biomechanical Strength Testing

In a comparative study with α -BSM™ and autograft as bone substitute materials in a canine femoral defect model, the biomechanical strength (torsion loading to fracture) of the samples were equivalent at each timepoint for this one year study.

3.3 Conclusions of Testing

The physico-chemical testing and biocompatibility evaluation performed on α -BSM™ Bone Substitute Material for Cranioplasty demonstrate that it is similar to the predicate device in terms of its chemical and crystalline composition, and that it shows an excellent biocompatibility and safety profile, with no significant adverse observations on any of a variety of subcellular, cellular, tissue, and systemic challenges.

For the above reasons, which are summarized in the following table comparing equivalence factors, ETEX believes that α -BSM™ Bone Substitute Material is substantially equivalent to BoneSource™ and possesses no properties which raise additional questions of safety relating to the intended use of the product.

COMPARISON TABLE OF SUBSTANTIAL EQUIVALENCE

α -BSM™ and BoneSource™

ITEM	α -BSM™	BoneSource™
Design	Self-setting calcium phosphate cement which hardens in aqueous environment at 37 °C	Self-setting calcium phosphate cement which hardens in aqueous environment at 37 °C
Composition, after hardening	Hydroxyapatite, with amorphous component	Hydroxyapatite, with amorphous component
Intended Use	Use in the filling, repair, reconstruction and augmentation of burr holes, contiguous craniotomy cuts, and other defects in craniofacial bones including fronto-orbital, malar and mental areas with a surface area no larger than 25cm ² .	Use in the repair of neurosurgical burr holes, contiguous craniotomy cuts and other cranial defects with a surface area no larger than 25 cm ² per defect. BoneSource is also indicated for augmentation or restoration of bony contour in the craniofacial skeleton including the fronto-orbital, malar and mental areas.
How Supplied	Sterile, nonpyrogenic powder contained in elastomeric mixing bulb to be mixed at time of implantation.	Sterile, nonpyrogenic powder contained in vial to be mixed at time of implantation.
Preparation Method	Sterile saline injected into mixing bulb, powder mixed by kneading bulb, paste removed and implanted.	Powder placed into mixing vessel, sterile solution added, powder mixed with spatula, paste implanted
Pot Life after mixing	Does not harden at room temperature, if moist	5 - 30 minutes dependent upon diluent
Hardening Time in body	One hour	Up to four hours
Solubility Product	6×10^{-54}	6×10^{-67}
Biocompatibility	Demonstrated	Presumed



NOV 25 1998

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Mr. Michael Schuttenberg
Director, Quality Assurance and Regulatory Affairs
ETEX Corporation
350 Massachusetts Avenue, 4th Floor
Cambridge, Massachusetts 02139

Re: K983009
Trade Name: α -BSM™ Bone Substitute Material
for Cranioplasty
Regulatory Class: II
Product Code: GXP
Dated: August 26, 1998
Received: August 28, 1998

Dear Mr. Schuttenberg:

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.

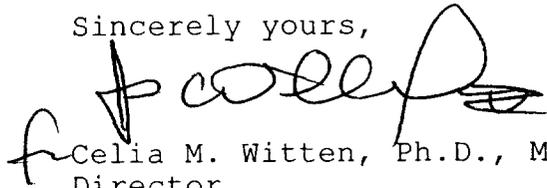
If your device is classified (see above) into either class II (Special Controls) or class III (Pre-market Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the current Good Manufacturing Practice 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 pre-market 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.

Page 2 - Mr. Michael Schuttenberg

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) 594-4659. 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 handwritten signature in black ink, appearing to read 'Celia M. Witten', with a stylized flourish at the end.

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

PREMARKET NOTIFICATION

DEVICE NAME AND INTENDED USE STATEMENT

Device Name: α -BSM™ Bone Substitute Material for Cranioplasty

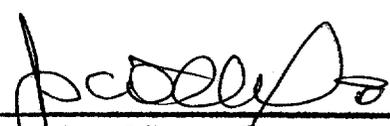
Indications/ Intended Uses:

α -BSM™ Bone Substitute Material is a synthetic calcium phosphate hydroxyapatitic material intended to be implanted for use in the filling, repair, reconstruction and augmentation of burr holes, contiguous craniotomy cuts, and other defects in craniofacial bones including fronto-orbital, malar and mental areas with a surface area no larger than 25cm².

PLEASE DO NOT WRITE BELOW THIS LINE--CONTINUE ON ANOTHER PAGE IF NECESSARY

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use X or Over-the -Counter Use _____



(Division Sign-Off)
Division of General Restorative Devices
510(k) Number 12983009