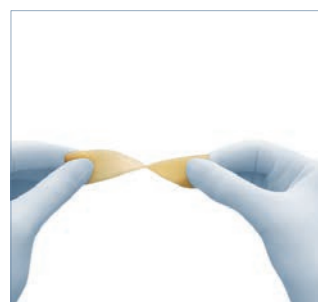


DBX™ – THE OSTEOINDUCTIVE POWER

- Proven osteoinductivity
- Careful processing
- Superior handling

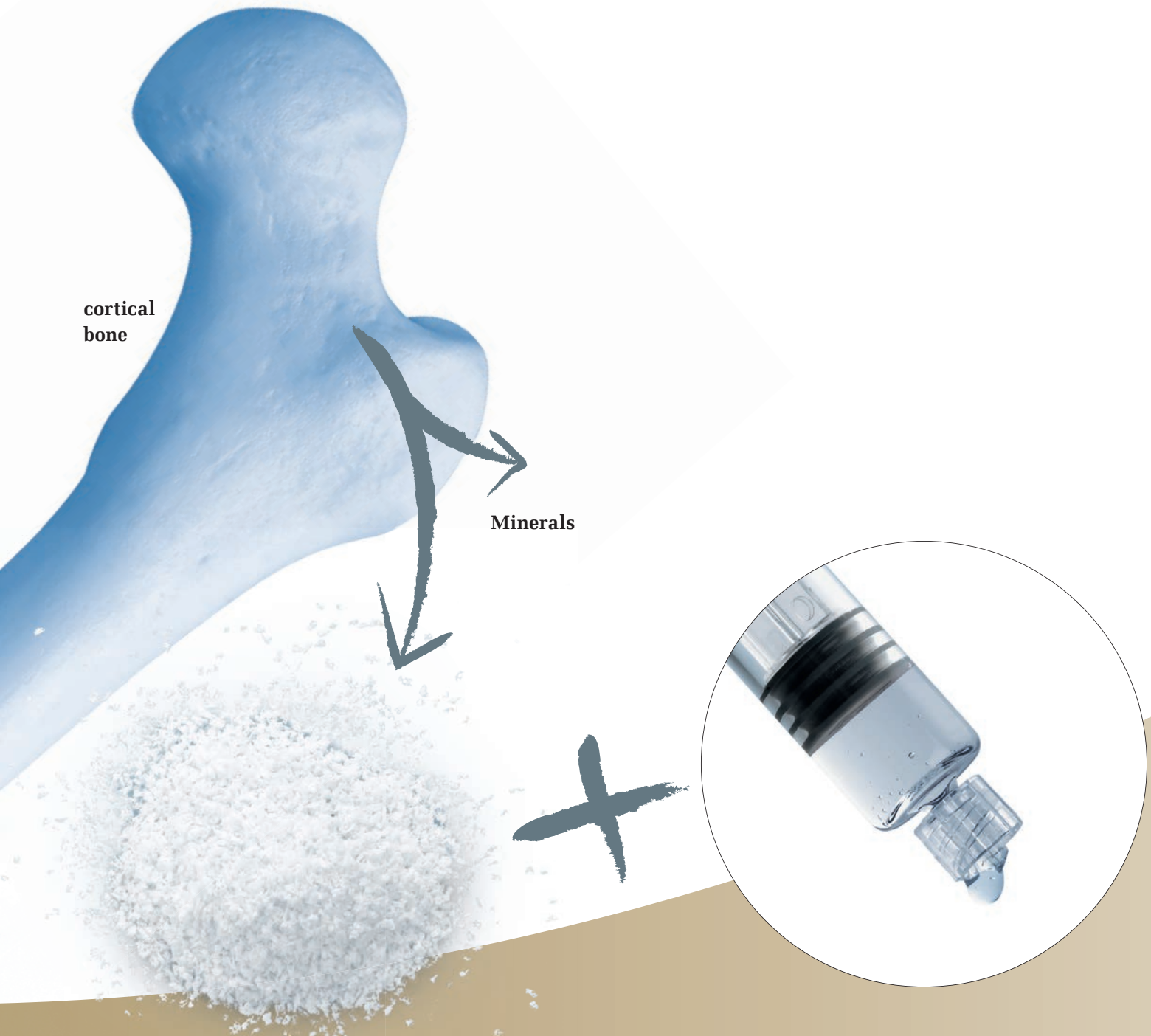


This publication is not intended for distribution in the USA.

AVAILABLE THROUGH
DEPUY SYNTHES

DBX™ BONE GRAFT SUBSTITUTE. THE OSTEOINDUCTIVE POWER.

DBX™ is demineralized bone matrix (DBM) from human donors combined with a biocompatible carrier.



The **demineralized bone powder** is produced by removal of minerals from cortical bone. It consists of collagen and bone growth factors such as bone morphogenetic proteins ^{2,3,4} (BMPs).

The **sodium hyaluronate** carrier present in DBX is designed to be isotonic and it models physiological pH. Sodium hyaluronate naturally occurs in the human body.

1 It is unknown how the osteoinductive potential, measured in the athymic mouse model or the alkaline phosphatase assay, will correlate with clinical performance in human subjects.

2 Reddi A.H. and Cunningham N.S. Initiation and promotion of bone differentiation by bone morphogenetic proteins. J Bone Miner Res 8 (Suppl. 2): S499-S502, 1993.

The various DBX™ tissue forms have been designed to meet surgical needs while maximizing the amount of bone delivered to the surgical site.



Proven Osteoinductivity

Every finished lot of DBX™ is tested for osteoinductivity prior to release. The bone growth factors present and active inside DBX are responsible for its osteoinductive potential.¹



Careful Processing

Processed by the Musculoskeletal Transplant Foundation according to standards among the most stringent in the industry.



Superior Handling

The addition of the sodium hyaluronate carrier provides superior handling to the various DBX tissue forms.



DBX Putty



DBX Mix



DBX Strip

DBX has osteoinductive potential¹.

³ Urist M.R. The search for and discovery of bone morphogenic protein (BMP) and Urist M.R., O'Conner B.T. and Burwell, R.G. Bone graft derivatives and substitutes. London: Butterworth Heineman: S315-S362, 1994.

⁴ Wozney J.M. The bone morphogenic protein family and osteogenesis. Mol Rep Dev 32: S160-S167, 1992.

DBX – Bone Graft Substitute.
The osteoinductive power.

INDICATIONS

DBX Putty and Mix

DBX Putty and Mix are intended for use as a Demineralized Bone Matrix for voids or gaps that are not intrinsic to the stability of the bony structure.

They are indicated for treatment of surgically created osseous defects or osseous defects created from traumatic injury.

DBX Putty and Mix can be used with bone marrow, autograft and allograft. DBX Putty, when used in the spine, can be used alone or mixed with autogenous bone (1:1 ratio by weight), or with bone marrow aspirate.

DBX Putty and Mix are for single patient use only.

DBX Strip

DBX Strip is indicated as a bone void filler for treatment of surgically created osseous voids or gaps that are not intrinsic to the stability of the bony structure.

It can be used in the pelvis, extremities, and the posterolateral spine for posterolateral fusion.

DBX Strip, when used for posterolateral spine fusion, may be used with autograft.

DBX Strip is for single patient use only.

Please refer to the Instructions for Use for complete description of indications, contraindications, warnings and precautions.

CLINICAL STUDIES

Clinical Study: Posterolateral lumbar fusion

A combination of DBX Putty and autograft was shown to be as effective as autograft alone in a multicenter, randomized, controlled clinical study of patients undergoing posterolateral spine fusion for the treatment of degenerative disc disease (DDD).

- Equivalent fusion rates were achieved:
 - DBX mixed with autograft = 100% at 24 months;
 - Autograft alone = 96% at 24 months.
- Both groups exhibited significant decrease in VAS pain scores at 6 months relative to baseline.
- The authors conclude that DBX Putty is at least as effective as autograft alone when used as a bone graft extender in the treatment of DDD via posterolateral spine fusion⁵.



Postoperative



24 months postoperative

Case study: Pseudoarthrosis of the distal tibia (pilon fracture)

A 29 years old patient suffered from a septic pseudoarthrosis of the tibial pilon, and an equinus deformity of the foot after 6 months from initial treatment of a pilon fracture.

Cleaning of the septic pseudoarthrosis, insertion of a gentamycin-containing PMMA cement, and correction of the equinus deformity were carried out.

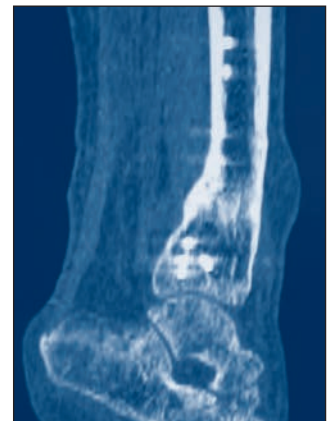
Definitive surgical treatment at 9 months after the initial injury included stabilization of the pseudoarthrosis, removal of the cement, and filling of the critical-size defect with a mix of 15 cc of DBX Putty and 5cc of autologous cancellous bone chips.

One year after surgery, complete consolidation of the pseudoarthrosis, regeneration of the defect with dense new bone and good articular function of the ankle joint was observed.

Surgeon: Dr. Dr. César Salcedo Cánovas, University hospital “Virgen de la Arrixaca”, Murcia, Spain.



6 months post-op: consolidation of the pseudoarthrosis and advanced progression of osteointegration.



12 months post-op: CT scan showing complete consolidation of the pseudoarthrosis and dense new bone at the defect site.

⁵ Becker, V., et al. Comparison of autograft to DBX demineralized bone matrix putty combined with autograft used in posterolateral lumbar fusion. AANS 73rd Annual Mtg, 2005.

DBX – Bone Graft Substitute.
The osteoinductive power.



PROVEN OSTEOINDUCTIVITY

DBX is processed using aseptic techniques eliminating the need for terminal sterilization methods⁶.

In addition, each lot of DBX is tested before release to ensure the osteoinductivity⁷ of the final product.

MTF uses one of two methods to prove DBX osteoinductivity. The *in vitro* method demonstrates the osteoinductivity of the DBX through the induction of alkaline phosphatase assay activity in live cells. This method has been validated to correlate with the *in vivo* athymic mouse method, which is based on the Urist model. In the *in vivo* method, DBX is implanted into the biceps femoris muscle of a nude athymic mouse. Histological slides are prepared from the implant after 28 days *in vivo*, and are evaluated for indications of new bone growth at the implantation site; the presence of indications of new bone growth establishes the osteoinductivity of the DBX.



In vivo athymic mouse method. X-ray 28 days post-operatively shows dense material indicating mineralization at the implant site (confirmed by histological findings)⁸.

⁶ Boyce, T., Edwards J. and Scarborough N. Allograft bone. The influence of processing on safety and performance. *Ortho Clin North Am.* 30:571–81, 1999.

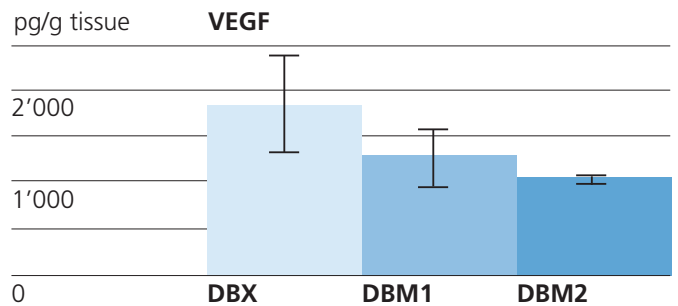
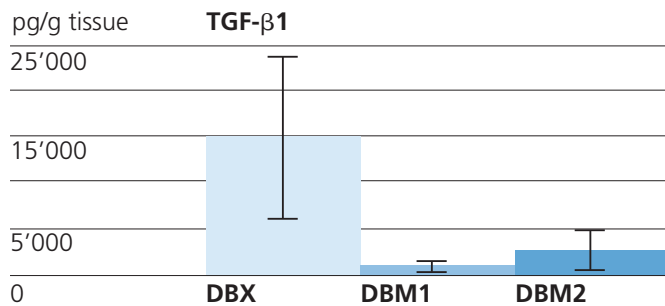
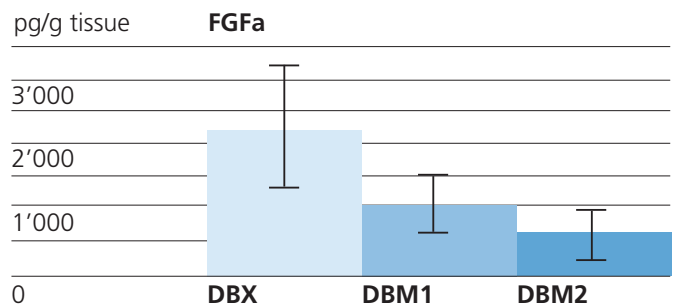
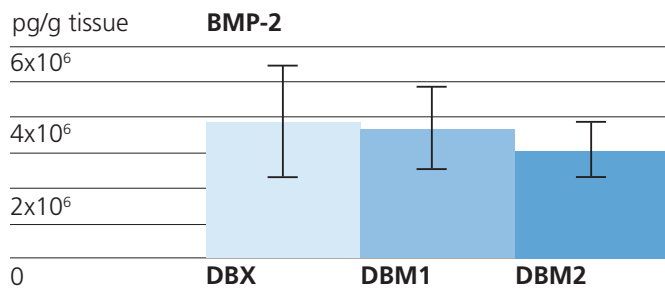
⁷ It is unknown how the osteoinductive potential, measured in the athymic mouse model or the alkaline phosphatase assay, will correlate with clinical performance in human subjects.

⁸ Gerzmann A.A., Sunwoo M.H. A pilot study evaluating sodium hyaluronate as a carrier for freeze-dried demineralized bone powder. *Cell and Tissue Banking* 2: S87–S9, 2001.

Quantification of growth factors

The content of specific growth factors, playing a central role in bone regeneration, was investigated in DBX and two other commercially available DBM-based products (DBM1, DBM2).

DBX showed higher quantities of TGF- β 1, FGFa and VEGF compared to the other analysed DBMs. Study: PD Dr. med. G. Schmidmeier, Centrum für Muskuloskeletale Chirurgie, Berlin, 2004.



DBX. Bone Graft Substitute.
The osteoinductive power.



CAREFUL PROCESSING

DBX is processed by the Musculoskeletal Transplant Foundation (MTF) in the United States and exclusively marketed through DePuy Synthes.

Founded in 1987, MTF is the leading non-profit tissue bank in the United States.

- MTF is dedicated to providing quality tissue through a commitment to excellence in education, research, recovery and care for recipients, donors and their families.
- Accredited by the AATB (American Association of Tissue Banks).
- Complies with all FDA and European regulations regarding the recovery, processing and distribution of allograft tissues.
- Certified according to ISO 13485.



Stringent donor selection

Every donor is screened thoroughly. Exclusion criteria for tissue donation include, but are not limited to infectious diseases, malignant diseases, neurological degenerative diseases, diseases of unknown aetiology and exposure to toxic substances.

Comprehensive testing

All tissue donors undergo stringent infectious disease testing, including tests for HIV-1, HIV-2, hepatitis B, hepatitis C and syphilis. HIV and hepatitis C are tested through NAT.

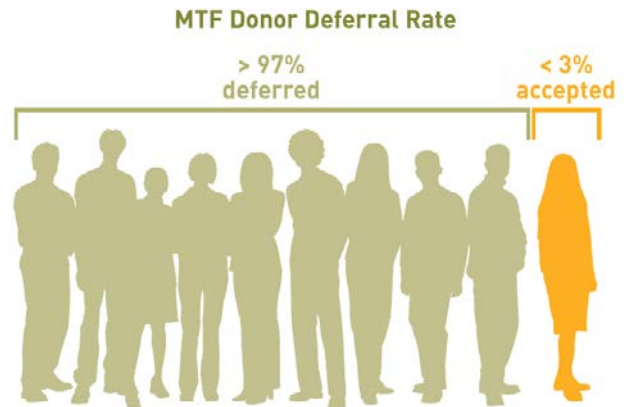
The tissue is microbiologically tested before and after processing.

Additional testing is performed as per country specific requirements.



Donor release

Donors are only released to processing after extensive review and sign-off of all charts and records by MTF's Medical Directors, who are all physicians with infectious disease or pathology backgrounds.



Processing: preserving tissue integrity

Tissues are aseptically processed in ISO class 4 certified clean rooms. Donors are not pooled: each donor represents a single batch. DBX is tested for sterility complying with the requirements of USP <71> Sterility Tests. MTF has provided over 6 million grafts for transplantation to date.

Viral inactivation

The manufacturing process of DBX has been validated to inactivate and clear a panel of viruses representing all virus types, modeling viruses such as HIV-1, Hepatitis C, cytomegalovirus/herpes (via pseudorabies virus (PrV)), Polio, and Human parvovirus B19 (via porcine parvovirus (PPV)).

DBX. Bone Graft Substitute.
The osteoinductive power.



EXCELLENT HANDLING PROPERTIES

A carrier with ideal characteristics

Sodium hyaluronate is a polysaccharide formed by plasma membrane proteins in the human body. It is naturally occurring in the human body in the joints, eyes, extracellular matrix of skin and musculoskeletal tissue. Sodium hyaluronate plays an essential role in cell proliferation, migration and adhesion and has been correlated to angiogenesis^{9,10}.

Sodium hyaluronate is proven to be safe. It confers positional stability to the tissue¹¹.

MTF uses high quality medical grade sodium hyaluronate, ISO 13485 certified, produced through fermentation processes under GMP guidelines.

The sodium hyaluronate used in DBX is designed to be isotonic and non-hemolytic and it models physiological pH.



⁹ Alicia Orlidge and Patricia A. D'Amore. Cell Specific effects of glycosaminoglycans on the attachment and proliferation of vascular wall components. *Microvascular Research* 31: S41–S43, 1986.

¹⁰ J. R. E. Fraser and T. C. Laurent T. Turnover and metabolism of hyaluronan. In: Evered D, Whelan J. eds. *The biology of Hyaluronan*. Wiley, Chichester (Ciba Foundation Symposium 143) S41–S59, 1989.

¹¹ Arthur Gertzman, Moon Hae Sunwoo. A pilot study evaluating sodium hyaluronate as a carrier for freeze-dried demineralized bone powder. *Cell and Tissue Banking* 2: S87–S94, 2001.

ORDERING INFORMATION

DBX Putty

93% DBM by volume combined with sodium hyaluronate and packaged in a glass syringe, not to be used as an applicator directly in the patient.

Art. Nr.	Volume (cc)
DBX-038005	0.5
DBX-038010	1
DBX-038025	2.5
DBX-038050	5
DBX-038100	10



DBX Mix

Provides a morselized cortical-cancellous bone texture combined with sodium hyaluronate. Eliminates or reduces the need to combine bone chips with DBM.

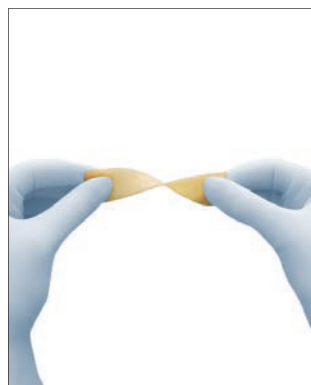
Art. Nr.	Volume (cc)
DBX-058025	2.5
DBX-058050	5
DBX-058100	10
DBX-058200	20



DBX Strip

Flexible Strip with no need for rehydration. DBM combined with sodium hyaluronate and porcine gelatin.

Art. Nr.	Size (in cm)
DBX-048015	1.5 × 1.5
DBX-048025	2.5 × 5
DBX-048010	2.5 × 10
DBX-048050	5 × 5



ALLOGRAFT SOLUTIONS REDISCOVER LIFE



An acknowledgement to the donor families of the incredible gift their loved one has made to others.

Donor Families often find comfort in getting a card or letter from the patient who received donated tissue.

Linking Lives is a voluntary program that gives tissue recipients the opportunity to write a message to the donor family. The letter is sent to MTF and then passed on to the donor family. Since the inception of this program over 15 000 letters have been written by U.S. tissue recipients. We are pleased to now extend this opportunity to tissue recipients outside the U.S.

Your patients will also be able to say 'thank you' to their donor families and let them know that their gift has improved the quality of life of others.

The new DBX package contains a **Linking Lives** insert which is given to the patient receiving the tissue: the insert includes instructions for participating in the program, a sample letter to the donor family and other information on MTF.

DBX allows for the butterfly of hope and new life to reach donor families.

MTF Musculoskeletal
Transplant
Foundation

THE ALLOGRAFT LEADER™

Facilitated through:
DePuy Synthes

This publication is not intended for distribution in the USA.