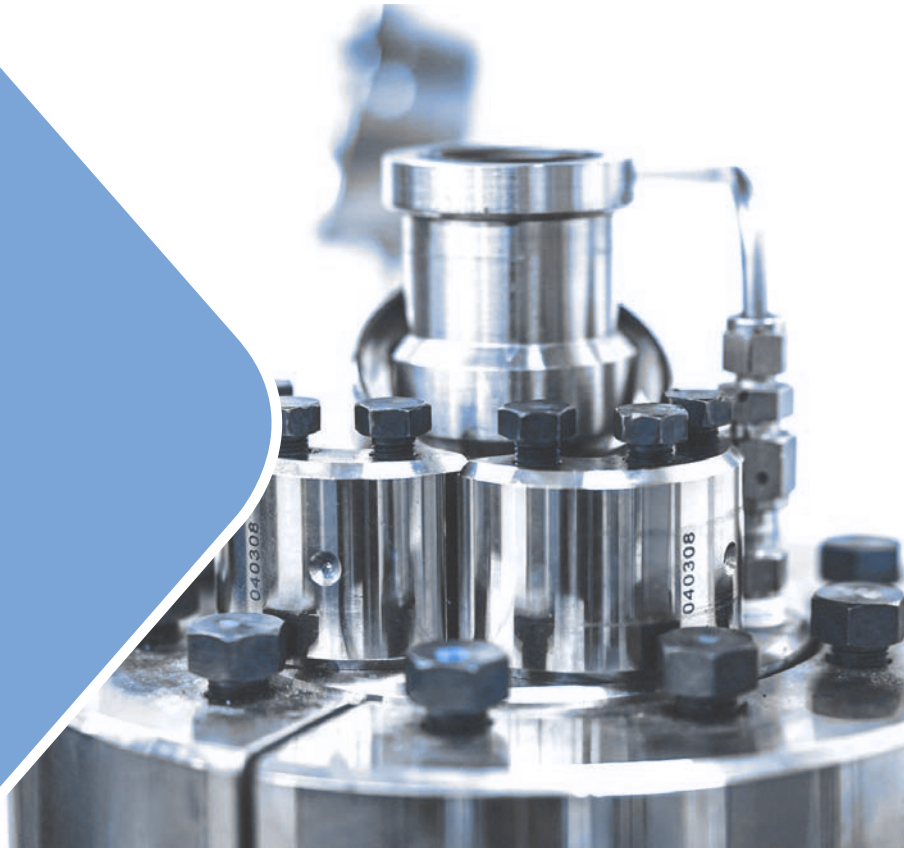
BIOBank
Preserved and regenerated human bone

BIOBANK BONE GRAFT

TECHNICAL BROCHURE



DENTAL RANGE

1. ORIGIN OF THE BONE GRAFTS

BIOBank is a French tissue bank authorised by ANSM (French National Safety Agency for Health Products) for the storage, transformation and distribution of bone grafts. The BIOBank grafts are human femoral heads (allografts) which have been taken from living donors during hip arthroplasties.

All samples are obtained in France by orthopaedic surgeons. Donors are selected on the basis of strict observation of health safety criteria, clinical criteria recommended by the French Biomedicines Agency and regulatory serological criteria.

The human femoral heads are converted into virally inactive sterile bone grafts using an exclusive, patented Supercrit® procedure based on the use of supercritical CO_2 which has "process/product" authorisations granted by ANSM.

2. PROCESSING STAGES

BIOBank uses Supercrit® process stages in its specially designed equipment laboratory with high performance clean rooms.

The Supercrit® process is based on an extraction technology using supercritical CO_2 (SC CO_2) to and decontaminate bone tissue. This technology is used in the pharmaceutical and farming-foodstuffs industries for fractionation, extraction and decontamination of biological materials (1). BIOBank is using the Supercrit® process for the first time in human bone tissue.

After mechanical removal of cartilage and osteophytes, the femoral head is subjected to the effect of CO_2 in the supercritical state under action of pressure and temperature. SC CO_2 has the viscosity of a gas and very powerful fat dissolution properties which provides it with its diffusion properties into bone tissue and extraction properties for fats contained in the bone trabeculae.

Through the SC CO_2, fat is completely removed from the humoral head regardless of the head dimensions with a final fat content of under 0.5%. In addition, the SC CO_2 is non-toxic, has antiviral activity (2) and its action on the bone, mineral and collagen framework is entirely neutral.

A chemical process is then used to complete the action of the supercritical CO_2:
- Hydrogen peroxide to oxidise residual proteins in the bone marrow,
- Molar soda to inactivate the prions pursuant to international regulations,
- Ethanol to dehydrate the bone tissue and ensure it is perfectly preserved.

Through the deep cleaning of the bone trabecular network with SC CO_2, the duration of action of these three solvents is shortened compared to conventional processes. The Supercrit® process does not therefore damage the bone tissue and achieves an extremely high level of viral safety.

Once perfectly deep cleaned, the grafts are then dried by simple hot air flow and packaged in a water-tight packaging sterilised by irradiation at 25 kGy. The long-term sterility of the products and their long term storage at room temperature is therefore guaranteed.

The Supercrit® process is a group of particularly effective mechanisms which respect the integrity of the trabecular bone tissue. The grafts are completely safe and preserve the mechanical resistance of fresh bone.

3. IN VITRO CHARACTERISATION

Viral Inactivation:

Viral inactivation has been assessed by the Pasteur-Texcell laboratory in two studies. The results demonstrate the effectiveness of the four stages of the Supercrit® process in inactivating the most resistant viruses, including Parvovirus, up to the heart of the complete femoral head (2, 3, 4).

Integrity of bone tissue characteristics:

- Biochemical analysis: mineral (Ca, P, Mg, Na) and organic composition (hydroxyproline, glycine, alanine and proline) identical to untreated bone tissue
- Scanning electron microscopy observation: complete removal of cellular and bone marrow cells preserving the conformation of collagen fibres
- Histological analysis: organic mineral framework and bone architecture unchanged
- Immuno-histochemical analysis: no denaturation of type I collagen

Effectiveness of cleaning:

- Lipid content reduced from 60% to under 0.5% without the use of toxic organic solvents
- Residual water content under 4%

Preservation of mechanical properties:

Three studies have been conducted to assess the influence of the Supercrit® process on the mechanical properties of the cancellous bone tissue:

- Compression tests in 2 paired series of 100 bone samples treated compared to fresh bone have demonstrated the biochemical parameters for the BIOBank bone grafts before sterilisation by irradiation, with a maximum rupture force of 10.2 ± 5.2 MPa and an elasticity module of 412 ± 149 MPa. No statistically significant difference was found with fresh bone (6).
- Ultrasound analysis of the influence of the dose of gamma irradiation has concluded that there is no difference between 10 and 25 kGy on the elasticity module of the processed dehydrated cancellous bone tissue compared to unirradiated fresh bone. In light of its efficacy this result adds to the demonstration of the benefit of this type of end-stage sterilisation for bone allografts (7).
- Different treatment processes on the cancellous bone have been compared with ultrasound analysis of matched samples before and after treatment. This shows that the Supercrit® process is a viral inactivation process which has least effects on the elasticity of cancellous bone tissue and therefore confirms its ability to optimise preservation of the structural and architectural qualities of the bone (8).

Storage conditions:

The BIOBank bone grafts have a shelf life of 5 years at room temperature.

4. ANALYSIS OF IN VITRO AND ANIMAL EXPERIMENTS

The toxicity tests have demonstrated the absence of toxic residues on the products after the process:

- Negative cytotoxicity test
- Negative systemic toxicity test
- No pyrogens
- Heavy metal content compliant with standard ASTM F 1088-87 (Pb≤30ppm-Hg≤5ppm)

The osteoconduction and tolerability in the intra-osseous site have been assessed in an implantation study in animals. Allogenic sheep bone (one treated series compared to an untreated series) was implanted on condylar site in 12 animals and analysed histologically at 1, 4 and 8 months (4 animals per period) to assess bone healing and tissue tolerance. The results demonstrate improved tolerance and superior and faster bone apposition for the processed samples. The quantitative parameters are all superior for the treated series demonstrating more active bone remodelling (4, 5).

5. PRESENTATIONS AND INDICATIONS

Forms and presentations:

The BIOBank bone grafts are available as different shapes tailored to the needs for bone regeneration in implant surgery and parodontology.

	Family	BIOBank bone grafts designation	Product code
	**Geometrical form**	Cancellous bone block 20x10x10 mm	90012
	**Cancellous bone powder « S » Granulometry 0.5 mm**	*Présentation en flacon :*	
		Volume 0.5 mm 0.5 cc	90031
		Volume 0.5 mm 1 cc	90032
		Volume 0.5 mm 2 cc	90033
		Volume 0.5 mm 4 cc	90034
		Présentation en seringue :	
		Volume 0.5 mm 0.5 cc	90035
		Volume 0.5 mm 1 cc	90036
		Volume 0.5 mm 2 cc	90037
	**Cancellous bone powder « L » Granulometry 1 mm**	*Présentation en flacon :*	
		Volume 1 mm 0.5 cc	90041
		Volume 1 mm 1 cc	90042
		Volume 1 mm 2 cc	90043
		Volume 1 mm 4 cc	90044
	**Cortico-cancellous bone powder « S » Granulometry 0.5 mm**	*Présentation en flacon :*	
		Volume 0.5 mm 0.5 cc	90051
		Volume 0.5 mm 1 cc	90052
		Volume 0.5 mm 2 cc	90053
		Volume 0.5 mm 4 cc	90054
		Présentation en seringue :	
		Volume 0.5 mm 0.5 cc	90055
		Volume 0.5 mm 1 cc	90056
		Volume 0.5 mm 2 cc	90057
	**Cortico-cancellous bone plates**	15x10x4 mm	90065
		20x12x4 mm	90066
	Cortical bone plates	12x10 mm	90063
		18x10 mm	90064

Therapeutic indications:

- The therapeutic indications for **cancellous and cortico-cancellous bone powders** are filling grafts for the maxillary with late functioning of the implants:
  - Peri-implant filling;
  - Filling to increase bone volume in the alveolar crest;
  - Filling for sinus elevation;
  - Post-extraction filling;
  - Filling for cystic cavity;
  - Filling of sampling site;
  - Filling of angular lesions in parodontal diseases.

- **The cortico-cancellous bone plates** are used as an alternative to autologous grafts (remove from the cranial site or sample from the iliac crest or endobuccal sample) before dental implantations in:
  - Insufficient bone volume of sinus floor;
  - Atrophic maxillary crests.

- **The cancellous bone block** is indicated for filling the sampling site and to increase the volume of alveolar crest bone.

- **The cortical bone plates** are indicated for increasing thickness of atrophic crests using the casing technique.

  Under conditions of substantial use and depending on the case in question, loading should be progressive.

6. PRESCRIPTION AND DISTRIBUTION

The BIOBank graft is provided on a **personal medical prescription** for single use. The patient must be informed of the use of tissue of human origin.

The prescription should be sent to BIOBank by the grafting surgeon prior to the surgery, by fax +33(0)1.64.42.59.60, or by email. The prescriber can use the model prescription form provided separately by BIOBank.

The information required for release of the grafts are:
- The name and contact details of the prescribing surgeon (RPPS no.)
- The name, age and sex of the recipient
- The date of the surgery
- The shape and amount of each graft prescribed
- The address where the grafts should be sent to.

7. INSTRUCTIONS AND PRECAUTIONS FOR USE

The BIOBank graft is dispensed for immediate use. It must not be frozen or refrigerated.

On receipt and before opening, the integrity of the outer packaging and inner packaging, shelf life of the graft and traceability documents must be checked.

The graft must not be used if the inner or outer packaging are not intact. If it is not used, the graft must be returned to BIOBank in its packaging.

Implantation of several combined grafts is the responsibility of the surgeon who must then pay greater attention to management of the traceability documents.

Operating procedure:

Open the inner packaging immediately before use, following aseptic conditions.

The bone powder in vial does not require rehydration as this is carried out on the grafting site. However, it promotes cohesion of the powder particles and facilitates manipulations.

Aseptic transfer allowed by the syringe presentation using the Luer-lock provided, a sterile 0.9% sodium chloride solution or the patient's blood, previously taken from the incision. It is preferable that a contact time of 2 to 3 minutes be left to optimise hold of the graft.

The cortical-cancellous bone plate, cancellous bone block and cortical bone plate must be rehydrated for 5 to 10 minutes in a sterile 0.9% sodium chloride solution and then adapted to the recipient's site. Height and length may be adjusted using a high speed bone drill bit with irrigation and using gouge forceps for thickness.

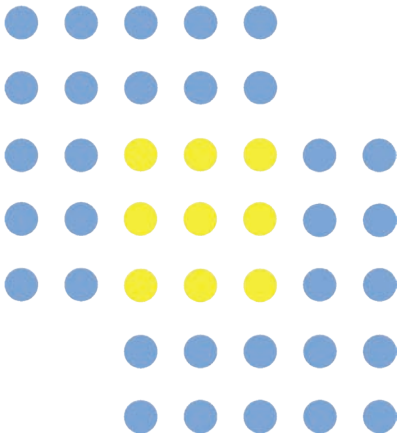
8. TRACEABILITY AND BIOVIGILANCE

To ensure traceability of each graft it is essential that the completed implantation form be returned to BIOBank and that the graft identity form be archived in the patient's records.

Any adverse effects due to or liable to be due to the product must be reported to the local biovigilance representative for the facility in which the product is used or failing this, to BIOBank.

9. BIBLIOGRAPHICAL REFERENCES

1. Fages J., Marty L., Delga C., Condoret J.-S., Combes D., Frayssinet P., Use of supercritical CO2 for bone délipidation. Biomaterials, 1994, 15: 650-6
2. Fages J., Frayssinet P., Poirier B., Barbier Y., Joffret ML, Larzul D., Majewski W., Bonel G., Viral inactivation of human bone tissue using supercritical fluid extraction. ASAIO Journal, 1998, 44: 289-93
3. Pasteur-Texcell, Evaluation of the viral safety level during manufacturing process of human bone grafts. Evaluation carried out by using the whole femoral head, Report number: 250/01/5375/01, 2003
4. Fages J., Jean E., Frayssinet P., Mathon D., Poirier B., Autefage A., Larzul D., Bone allografts and supercritical processing: effects on osteointegration and viral safety. The Journal of Supercritical fluids, 1998 13: 351-6.
5. Frayssinet P., Rouquet N., Mathon D., Autefage A., Fages J., Histological integration of allogeneic cancellous bone tissue treated by supercritical CO2 implanted in sheep bones. Biomaterials, 1998, 19 : 2247-53
6. Mitton D., Rappeneau J., Bardonnet R., Effect of a supercritical CO2 based treatment on mechanical properties of human cancellous bone. Eur J Orthop Surg Traumatol, 2005, 15: 264-9
7. Vastel L., Masse C., Crozier E., Padilla F., Laugier P., Mitton D., Bardonnet R., Courpied J.-P., Effects of gamma irradiation on mechanical properties of defatted trabecular bone allografts assessed by speed-of-sound measurement. Cell Tissue Banking, 2007, 8:205-10
8. Vastel L., Masse C., Mesnil P., Crozier E., Padilla F., Laugier P., Mitton D., Courpied J. P. Comparative ultrasound evaluation of human trabecular bone graft properties after treatment with different sterilization procedures. J Biomed Mater Res B Appl Biomater. 2009 Jul;90(1):430-7



BIOBank

3 rue Georges Charpak
77127 Lieusaint
FRANCE

Tél. +33 (0)1 64 42 59 65
Fax +33 (0)1 64 42 59 60

commercial@biobank.fr
www.biobank.fr

9-01-BT1-GB
Rev A/06.19